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IMPORTANCE OF DIAGNOSTIC METHODS IN PHYSICAL MEDICINE

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Great advances in physical medicine and rehabilitation have been made in recent years, but there is still a lack of appreciation of the importance of diagnostic procedures; yet diagnosis was one of the earliest activities of men working in the field of physical medicine. Jallibert first induced muscle contraction by electric spark in 1732. Thus began the use of electrical currents in the diagnosis of neuromuscular disorders. In 1786 Galvani produced muscle contraction by the constant current, and later Remak determined the location of motor points so accurately that they are still used today. Further advances in the diagnostic use of electric current have run apace with the development of our knowledge of electricity in general. The treatment of peripheral nerve lesion is an important part of our work in physical medicine, and the advances made in the diagnosis and prognosis of nerve lesion has been of immense importance in determining the treatment of this condition. A large number of the casualties of both world wars were peripheral nerve lesions, and industrial injuries include an even larger percentage of these lesions. An accurate knowledge of the exact condition of the nerve supplying a muscle leads to correct treatment and better prognosis. It is also important in determining whether a nerve suture is necessary and the exact time to do it and whether the nerve repair has been successful, thus saving months of waiting to see if the muscle will regain its contractility.

QUALITATIVE TEST

The oldest muscle test was the reaction of degeneration, which is purely a qualitative test and tells only that there is a lesion of the nerve but does not tell the extent of the lesion. It is a simple test, easily done, and of much practical use today. There are many general neuromuscular diseases in which there is muscle weakness either localized or general, and the reaction of degeneration will aid in diagnosis by determining whether the condition is due to a central lesion or a lesion of the peripheral nerve.

There are four criteria that explain the use of reaction of degeneration: 1. A muscle will not contract to interrupted faradic current unless the nerve is intact. 2. In a normal muscle with intact nerve the negative closing contraction of the galvanic current is greater than the positive. 3. Any change from this normal formula constitutes a reaction of degeneration. Either the negative and positive contraction become equal or there is a revisal of form where the positive becomes greater than the negative, and in a complete reaction of degeneration there is no contraction to either the negative or positive stimulation. 4. Whenever the reaction of degeneration is present the lesion is in the peripheral motor neuron.

QUANTITATIVE TEST

It soon became evident that we also needed a quantitative test, and the earliest one was the condenser method of testing. A series of condensers of known capacity was used. The correct condenser to produce a contraction was determined. At subsequent testing if a greater capacity was required to produce a contraction it meant the degeneration was increasing, whereas if a lesser capacity produced a contraction the nerve was regenerating. This gave us a quantitative test and roughly enabled us to determine the progress of regeneration. A more accurate quantitative test for nerve degeneration was the chronaxy test developed by Lapicque. Chronaxy is the time required for the excitation of a nerve or muscle by a definite stimulus. The smallest amount of current without regard to its duration that will produce the smallest perceptible contraction is determined. This is called the threshold of excitation, or rheobase. This threshold of excitation is doubled. Once this is obtained the length of times it must act to produce a contraction is determined. An apparatus is used that accurately determines the time, usually measured in 0.001 second and called sigma. A normal muscle will respond in 0.00067 second, whereas a degenerating nerve may require 0.01, 0.05, or even 0.1 second. It is possible in this way to determine the amount of degeneration present and to check any increase or decrease in the degenerative process. The elevation of muscle chronaxy is significant of lower motor neuron pathology. Damage above the lower motor neuron produces no elevation of chronaxy nor does direct muscle damage. Elevated values may be expected in cases of poliomyelitis, spinal

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atrophy, amyotrophic lateral sclerosis or acute ascending myelitis (Landry's paralysis), spinal cord tumors, pressure from disk lesions, laceration of nerve, or toxic neuritis. Disseminated chronaxy changes are present in cases of multiple sclerosis or syringomyelia.

OTHER TESTS

A number of other diagnostic tests are being used, and their importance and reliability will be definitely determined by further clinical experience.

The strength duration curve is obtained by plotting the current required to produce the same degree of contraction as was observed in the determination of the rheobase against a series of decreasing stimulus durations. When normal it should show a continuous flat slope (during degeneration there is a discontinuous steep slope). When denervated there is a continuous steep slope that on regeneration becomes discontinuous again. Chronaxy will be a point of reference on the strength duration curve. This test has its value as a prognostic sign.

The galvanic tetanus ratio is defined as the quotient obtained by dividing the value of galvanic current required to produce a tetanus by the value of current required to produce a minimal contraction (rheobase). A normal muscle requires three to six times as much current to produce tetanus as the rheobase. A degenerating muscle shows a gradual approach to unity. A completely degenerated muscle shows a ratio of 1 to 1.5. As the muscle regenerates it shows a ratio of 10 or more and is a good indication of regeneration. The galvanic tetanus ration must always be considered in relation to the time interval between the injury and the examination.

Another test that is being used is repetitive stimuli or strength interval curve. A tetanic contraction of a muscle is produced by a series of direct current stimuli having short duration separated by short intervals. The short stimuli is not effective of itself but produces a state of hyperexcitability and when rapidly repeated leads to contraction of the muscle. This is most effective in normal muscles but rapidly diminishes when the interval is increased. If the muscle is denervated, the strength of the stimulation must increase markedly. The curve ascends during nerve degeneration and flattens out during regeneration, rendering important prognostic information.

The following findings have been suggested in neuromuscular examination: evidence of degeneration shown by (1) galvanic tetanus ratio near 1.00, (2) repetitive stimuli requiring progressively greater amounts of current as the interval between stimuli is increased, (3) chronaxy above 15 milliseconds, (4) strength duration curve steep and continuous in the region of long duration, and (5) rheobase ratio of 1.0 or less; evidence of regeneration shown by (1) galvanic tetanus ratio greater than 1.5, (2) repetitive stimuli requiring only slight increase in amount of current, (3) chronaxy below 15 milliseconds, (4) strength duration curve discontinuities, and (5) rheobase ratio of 1 to 3; and normal muscle shown by (1) galvanic tetanus ratio 3.5 to 6.00, (2) repetitive stimuli requiring about the same amount of current for 1, 5, or 10 milliseconds, (3) chronaxy below 1 millisecond, (4) strength duration curve continuous, and (5) rheobase ratio of 1.5 to 3.00.

DIAGNOSIS OF NEUROMUSCULAR DISEASES

Further studies in the diagnosis of neuromuscular diseases have resulted in the perfection of the electromyograph and the establishment of fibrillation as an objective clinical finding. The electrical recording of fibrillation of degeneration action potentials is now accepted as a definite adjunct to clinical medicine. The electromyograph picks up and amplifies electrical voltages in a muscle and reproduces them on an oscilloscope, renders them audible through a loud speaker, and then records them on a tape recorder. The visible patterns can be photographed on the oscilloscope. The electromyograph should be operated in a fully screened room to exclude extraneous wave lengths. Skin electrodes were used at first, but today the needle electrode is much more accurate. These needles are insulated except for the tip and are inserted into the muscle to be examined. The relaxed normal muscle is electrically silent and develops no voltages that can be recorded. On contraction of a normal muscle, normal motor unit voltages are elicited. This represents the contraction of a functional unit consisting of one anterior horn cell, its axon, and 100 to 150 muscle fibers that it enervates. This contraction is synchronous and can easily be recognized by its sound and appearance. When a voluntary muscle is denervated for a period of time, invisible rhythmic twitching of the muscle occurs, and so-called denervation fibrillation voltages appear on the electromyograph. These denervation fibrillation voltages are important, as they are significant of peripheral nerve injury and disappear when the nerve regenerates. They also disappear when the muscle is fibrosed. They are the most important findings shown by the electromyograph.

Polyphasic motor unit voltages occur during degeneration and during regeneration and represent the asynchronous contraction of abnormal muscles and are of prognostic importance in the regenerating stage. Fasciculation voltage is the visible involuntary contraction of a simple motor unit and has a characteristic sound and appearance. When the contractions appear alone they have no clinical application as they are recorded from normal muscles at times.

In patients with myotonia there are outbursts of motor voltages that sound like a diving airplane and are quite characteristic, making the diagnosis quite simple. The electromyograph is a fairly accurate clinical procedure when used by one who has the experience to properly evaluate the various voltages. It is particularly valuable in all cases of lower motor involvement and will aid in the diagnosis of many general conditions where lower motor pathology is present. It is of aid in localizing cases of spinal root compression, poliomyelitis, multiple sclerosis, tabes dorsalis, scalenus anticus syndrome, cervical rib, and many other conditions in which the peripheral nerve is involved.

The physiatrist has at his command a number of tests that are of extreme clinical value from both the diagnostic and prognostic view. In view of the frequency of peripheral nerve injuries in war and peace and of

the many generalized conditions in which peripheral nerves are involved, these clinical examinations must be of ever-increasing importance in the practice of physical medicine and rehabilitation.

The diagnosis of hysterical paralysis is frequently a dangerous procedure and one that should only be made after a careful examination utilizing all the tests to disprove it. There is no way a hysterical patient can deceive these various electrical tests, particularly the electromyograph. Too many cord tumors have been thus misjudged until the pathology was irreversible and permanent damage had been done. A similar situation occurs with malingering cases, particularly in industrial accidents where the patient is making unwarranted claims of permanent injury. Insurance companies find that an early neuromuscular study will frequently save them much in damage claims. Malpractice suits can be successfully defended when definite evidence of the lack of neuromuscular damage can be presented. Neuropathies frequently present great difficulty in diagnosis, and definite evidence, such as can be obtained by these various tests, is of great aid in establishing an early diagnosis and instituting early and correct therapy.

Localization of disk lesion by the electromyograph is assuming more importance and as experience increases much dependence will be placed on the evidence presented. The myelogram is not the most accurate test in such cases, and where two disks are involved it frequently results in additional operation procedures. Persistent neck and shoulder pain is now being shown to be due in many cases to nerve root pressure from exostosis in patients with cervical arthritis and explains the difficulty in relieving many of the patients. Pains and weakness, resulting from toxic neuritis due to lead or arsenic, if discovered early, will have an important bearing on the prognosis.

Muscular dystrophies present a group of conditions in which the diagnosis is complex and difficult. Progressive muscular atrophy if neural in origin will show a proportionately diminished number of action potentials depending on the degree of atrophy and the presence of fibrillation. If the condition is due to a slowly advancing degenerative disease of the muscle, the motor neuron is unaffected and the result will be a diminishing of the number and size of the motor units but no fibrillation will be found. The electromyograph is a welcome help in solving the problem of muscle weakness.

COMMENT

Neuromuscular conditions are numerous and common but are frequently attended with difficulty in diagnosis so that any help is greatly appreciated. The tests we have available are capable of giving us this aid. When understood and generally used they will be of inestimable help in the early diagnosis and proper treatment of these conditions. Every hospital has need of this service, and the physical medicine department should be prepared to meet the need and thus greatly extend its usefulness as an important branch of the practice of medicine.

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TAMPON METHOD FOR MASS SCREENING TO DETECT CARCINOMA OF CERVIX UTERI

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In November, 1954, Dr. Alexander Brunschwig [1] described the trial of a method for cytological detection of carcinoma of the uterine cervix by the use of a specially designed vaginal tampon. The concept of such a mass screening for early cancer detection originated with Dr. Andre Draghi, who designed a special vaginal tampon to implement that technique. This tampon consists of a tightly compressed cylinder of cotton partially encased in a sheath of nylon (see figure). A group of 227 patients were studied by this screening method by Dr. Brunschwig. He concluded from this study that the method appeared to be feasible but felt that the evaluation of the method must await an actual large-scale trial.

The cytological evaluation of the smears made from the 227 patients studied by Dr. Brunschwig was done by Dr. George N. Papanicolaou.[2] Dr. Papanicolaou felt that the analyzed results of the tampon smears compared favorably with the results obtained by the examination of smears prepared by the standard aspiration technique. He felt that, although the tampon method does not provide as adequate material for cytological study as a set of vaginal and endocervical smears, nevertheless, it had certain advantages, such as a greater purity of smear, that aided markedly in the screening as well, in addition to presenting a smear that contained fresher cells and was relatively free of decaying cells, bacteria, and detritus. He concluded that the Draghi detection tampon appeared suitable for mass screening purposes but that for final diagnosis we must still depend upon thorough gynecologic examination and biopsy.

On the basis of the studies carried out by Drs. Brunschwig and Papanicolaou, it seemed advisable that further studies be done on a larger number of patients to evaluate this method for mass screening of large groups of the female population for the early detection of carcinoma of the uterine cervix. Accordingly, at the request of Dr. Draghi, such a study was started on Feb. 7, 1955, at University Hospitals, Madison, Wis. During the period of time from Feb. 7, 1955, until Sept. 1,

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The Draghi detection tampons used in this study were supplied by Tampax, Inc., Palmer, Mass.

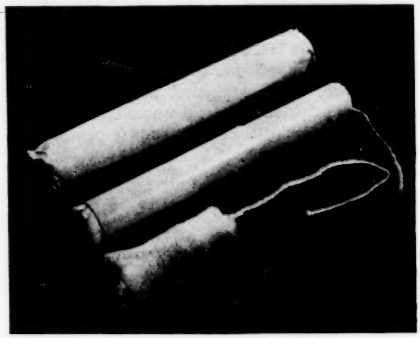
1. Brunschwig, A.: A Method for Mass Screening for Cytological Detection of Carcinoma of the Cervix Uteri, Cancer 7: 1182-1184 (Nov.) 1954.

2. Papanicolaou, G. N.: Cytological Evaluation of Smears Prepared by the Tampon Method for the Detection of Carcinoma of the Uterine Cervix, Cancer 7: 1185-1190 (Nov.) 1954.

1955, 2,059 patients have been screened by the use of the Draghi detection tampon for the cytological detection of carcinoma of the cervix uteri. A detailed account of the program as it developed and an analysis of the results of the study follows.

TECHNIQUE

At the onset of the study, during the first weeks, the patients screened by this method were (1) clinic and private patients seen in the outpatient gynecologic clinic; (2) patients seen in the gynecologic clinic in consultation for the other services of the hospital, including hospitalized patients as well as outpatients; and (3) gynecologic tumor clinic patients, most of whom had received some type of radiation therapy or had had extensive major surgery for a known malignant neoplasm in the pelvis, cervix, uterus, or ovaries. At the time that these patients reported to the clinic, each one was given a detection tampon to insert into the vagina. Prior to doing a bimanual pelvic examination on these patients, the



Draghi detection tampon.

tampon was removed from the vagina by the examiner and the smear made by stamping the tampon on the slide, rotating it on the slide, and rubbing the side of the tampon on the slide. The slide was then placed immediately into the fixative solution. In this group of patients, the length of time that the tampon remained in the vagina varied from 10 minutes to one hour.

Until some experience had been gained in the use of the method and some evaluation of the smears had been made, it was decided to take a routine suction-type of smear as well as a tampon smear on each patient. The two smears were compared by the cytologists, who reported that the tampon smear was a satisfactory smear after a double check had been done on 154 patients. After this approval from the laboratory, with few exceptions, the tampon smear was the only smear taken on all other patients included in this study. As Drs. Brunschwig and Papanicolaou had pointed out that the smear obtained from the tampon was superior if the tampon had remained in the vagina overnight, this study was expanded on Feb. 15, 1955, to include all inpatients admitted to the gynecologic ward of the hospital. Further expansion was carried out when, on March 25, 1955, all admissions to the women's surgical ward were included, and, on May 5, 1955, all admissions to the two women's medical wards were included.

The instructions placed on each ward for the use of the detection tampons were as follows: 1. No vaginal examination is to be done on the patient prior to the insertion of the tampon. Make certain that the patient has not had a vaginal douche in the 24 hours preceding the insertion of the tampon. 2. On the night of the day of admission of the patient to the hospital, the patient is to insert the tampon into the vagina. No lubricant is to be used. 3. The tampon is to remain in the vagina until the next morning. 4. The patient is to remove the tampon the next morning in the presence of a nurse, who will make a smear on the Papanicolaou slide immediately and then will place the slide into the bottle of fixative solution immediately. 5. All Papanicolaou laboratory slips on these patients must have the following information on them: (*a*) name of patient and her age, (*b*) history number, (*c*) date on which smear was obtained, (*d*) ward on which patient resides, (*e*) any pelvic symptoms, (*f*) if known carcinoma of the cervix is present or patient has had any pelvic irradiation, so state on the slip. 6. Instructions for making smear: Exert digital pressure on the tampon with thumb and forefinger and stamp tampon on the slide, making a slight clockwise rotation of the tampon on the slide as the smear is made. In addition, rub the sides of the tampon on the slide. Place the letter T on the identification tab on the slide so that the laboratory will know that the smear was made by the use of a tampon.

A nurse on duty on the ward during the hours of 7 to 11 p. m. was assigned to the duty of assuring that each patient inserted the tampon into the vagina. Another nurse made rounds on these patients the following morning and made the smear from the tampon given to her by the patient. Data, as follows, were recorded by the nurse on the data sheets kept on the ward: (1) history number, (2) name of the patient, (3) age of patient, (4) any pelvic symptomatology, and (5) date on which the smear was made. All reports were received from the cytological laboratory, where the laboratory number of the slide and the cytologist's report were recorded on the data sheet.

Some problems were encountered in the use of the tampon by the patients. Many of the patients in the older age group were not familiar with the use of vaginal tampons; therefore, it was necessary for the nurse or attendant to instruct the patient as to how to insert the tampon into the vagina. In a few of the patients in the younger age group, the size of the tampon seemed to account for some difficulty of insertion into the vagina. At my request, a medium size and a junior size tampon with the nylon cover were made to overcome this difficulty. The smears made with the smaller size of the tampon were satisfactory; however, it was felt that when the larger size could be used it was to be preferred, as a greater amount of secretion would be available for the smear. A few of the patients in the postmenopausal era experienced some difficulty in inserting the tampon because of the dryness of the vagina. It was in this group

of patients that the tampon proved of particular value, however, as no material for a smear could be obtained by the suction method.

As the program has continued there has been less difficulty as far as knowledge of the use of the tampon is concerned. This has been noted especially in that group of patients who report to the tumor clinic for examination every two months. In the interval of time during which this study has been carried out, most of these patients have had three Papanicolaou smears made by the method with use of the Draghi detection tampon. Since the first visit to the clinic, when the tampon method was used, they have become familiar with the use of the tampon and do not need further instructions at subsequent visits.

RESULTS

The cytologists reported all smears according to the following categories: 1. No malignant cells are noted. 2. Atypical cells present suspicions of malignant cells, recommend further study. 3. Malignant cells present. 4. Quantity insufficient to be of diagnostic value.

From the onset of the study on Feb. 7, 1955, to its completion on Aug. 31, 1955, a total of 2,059 patients were screened for the cytological detection of carcinoma of the cervix uteri by the use of the Draghi detection tampon. Of these patients, 1,301 had the tampon left in the vagina for a relatively short period of time, i. e., 10 to 45 minutes. Seven hundred fifty-eight patients had the tampon left in the vagina overnight.

In the entire group of 2,059 patients, 25 (or 1.2%) had smears reported "malignant cells present," 6 (or 0.3%) had smears reported as suspicious, 28 (or 1.36%) had smears reported "unsatisfactory, insufficient material on slide for diagnostic purposes," and 28 (or 1.36%) had smears reported "Trichomonas present." Of the 25 patients who had a positive smear reported, 9 had known cases of carcinoma of the cervix and were being seen in the gynecologic tumor clinic; 2 had adenocarcinoma of the fundus uteri confirmed by a diagnostic curettage; 12 had squamous cell carcinoma of the cervix confirmed by a cervical biopsy; one had a known primary carcinoma of the vagina confirmed by a previous biopsy of the vaginal mucosa; and one had a known squamous cell carcinoma of the cervix, grade 4, previously treated with x-ray and radium. In the last-mentioned patient a biopsy of a suspicious recurrent lesion of the cervix was reported by the pathologist as "indeterminate." In the six patients on whom the tampon smear was reported as suspicious, although further study by biopsy was advised, to date this has been done in one instance only. In the one patient on whom biopsy was done, the biopsy report was negative. One of the other five patients had a known case of squamous cell carcinoma of the cervix and had received a full complement of radiation therapy. Further study by biopsy has been advised on the other four patients, and it is expected that this will be done in the near future.

It is customary in the University Hospitals for the staff of the gynecologic service to examine many patients in consultation for the other services in the hospital. If pelvic pathology is found, proper therapy is recommended. The therapy recommended may be carried out in this hospital or, if the patient has been admitted for diagnosis only, the therapy may be carried out by the referring physician in some other community in the state. During the interval of time over which this study was made, 147 (or 7.1%) of the 2,059 patients had a dilation and curettage and/or biopsy of the cervix done because of the presence of pelvic pathology. While this may appear to be a low incidence of biopsy, it must be remembered that the total number, 2,059, of patients were screened as a routine procedure on the medical and surgical and gynecologic wards and that the great majority of the patients admitted to the medical and surgical wards did not have pelvic examinations done by the staff of the gynecologic service.

Comparison of Pathological Diagnosis and Cytological Report

Group	No. of Patients	Negative Smear Negative Biopsy		Positive Smear Positive Biopsy		Agreement		Negative Smear Positive Biopsy		Suspicious Smear Negative Biopsy		Unsatisfactory Smear Negative Biopsy		Positive Smear Indeterminate Biopsy		Non-agreement	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Tampon in overnight	62	51	82.25	3	4.84	54	87.09	6	9.67	1	1.61	1	1.61	..	....	8	12.9
Tampon in short time	85	74	87.06	5	5.88	79	92.94	5	5.88	..	....	..	....	1	1.18	6	7.06
Total	147	125		8		133	90.5	11	7.48	1	0.68	1	0.68	1	0.68	14	9.5

A comparison of the pathological diagnosis of the tissue obtained by biopsy with the cytological report of the tampon smear on these 147 patients yielded the information as shown in the table. In 133 of the 147 patients the results of the biopsy confirmed the cytological report of the smear. One patient had a suspicious smear and a negative biopsy, one patient had a smear that was reported as unsatisfactory and a negative biopsy, and one patient had a positive smear and a biopsy that was reported as indeterminate. Eleven patients had a negative smear reported by the cytologist and a positive biopsy reported by the pathologist. Therefore, the cytological report on the detection tampon smear agreed with the biopsy in 90.5% in this group of 147 patients and failed to agree in 9.5%. While it was not possible to determine why it was that 11 patients, 7.48% of the 147 patients, had negative smears with a positive biopsy, the following brief analysis of these cases may present some pertinent facts.

REPORT OF CASES

CASE 1.—On two occasions a suction smear and a tampon smear were reported as negative for malignant cells. Diagnostic curettage revealed the presence of adenocarcinoma of the fundus uteri of low-grade malignancy.

CASE 2.—Suction smear reported as showing presence of malignant cells; tampon smear reported as no malignant cells noted. This patient had a primary carcinoma of the bladder.

On biopsy a lesion on the vaginal wall was diagnosed as papillary adenocarcinoma arising in the bladder.

CASE 3.—Suction and tampon smears were reported negative for malignant cells. On curettings a diagnosis of adenocarcinoma of the fundus uteri was made.

CASE 4.—Suction smear taken by intern at time of admission examination was reported as showing malignant cells present. Three tampon smears taken subsequent to this were reported as negative. On biopsy of the cervix a diagnosis of carcinoma in situ of the cervix was made.

CASE 5.—The referring physician reported two positive suction Papanicolaou smears followed by two negative cervical biopsies on this patient prior to her admission to the hospital. On May 2, 1955, on circumferential cervical biopsy a diagnosis of carcinoma in situ was made. Tampon smear on May 3, 1955, was reported as negative. Total hysterectomy was done on May 9, 1955, and carcinoma in situ in the cervix uteri was reported.

CASE 6.—The referring physician reported squamous cell carcinoma of the cervix diagnosed by biopsy of the cervix done by him 13 days prior to the admission of the patient to this hospital on May 9, 1955. A tampon smear on May 10, 1955, was reported as showing no malignant cells. On biopsy of the cervix on May 10, 1955, a diagnosis of squamous cell carcinoma of the cervix, grade 4, was made. On pelvic examination the lesion was diagnosed as squamous cell carcinoma of cervix uteri, stage 3. As this patient was a schizophrenic and difficult to control, further tampon smears were not attempted.

CASE 7.—On April 27, 1955, two weeks prior to the admission of this patient to the hospital a biopsy and cauterization of the cervix and the implantation of 2,400 mg.-hr. of radium into the cervix had been done by the referring physician. Tampon smear on May 11, 1955, was reported as negative. On biopsy of the cervix on May 12, 1955, a diagnosis of squamous cell carcinoma of the cervix uteri, grade 2, was made.

CASE 8.—This patient had had a biopsy and cauterization of the cervix done three days prior to her admission to the hospital and entered with a diagnosis of squamous cell carcinoma of the cervix. Tampon smear made on the morning following the day of admission was reported as no malignant cells noted. On biopsy of the cervix done on the same day, a diagnosis of "clusters of neoplastic epithelial cells in depth of tissue—squamous cell carcinoma, grade 3," was made. Subsequent tampon smears done 5 and 10 days later, respectively, while the patient was receiving deep x-ray therapy were reported as negative for malignant cells.

CASE 9.—Pelvic examination on a 71-year-old woman who denied any pelvic symptoms showed a small polyp present in the cervix and some hyperplasia of the epithelium in the cervical canal. Tampon smear was reported negative, but a spatula smear of cells scraped from the cervical canal showed malignant cells present. On biopsy of the cervix with removal of the polyp a diagnosis of benign cervical polyp, carcinoma in situ of cervix uteri, was made.

CASE 10.—A patient had a known squamous cell carcinoma of the cervix, which had been diagnosed and treated by x-ray and radium elsewhere three years prior to her admission to the hospital. Tampon smear was negative. Biopsy of the cervix showed carcinoma still present.

CASE 11.—This patient was admitted on Feb. 28, 1955, with a known diagnosis of squamous cell carcinoma of the cervix, which had been treated elsewhere with 6,100 mg.-hr. of radium. Tampon smear done on the morning of March 1, 1955, was reported as negative. Pelvic examination done later that same morning showed the upper portion of the vaginal vault occluded by an adhesive vaginitis with some nodular tissue palpable through the adhesions. The pathologists report on this patient was as follows. On review of slides of April 22, 1953 (obtained from hospital where patient received radium therapy) a diagnosis of squamous cell carcinoma, grade 3, was made. On vaginal biopsy, done on March 2, 1955, the sections showed a heavy layer of fibrous superficially crusted granulation tissue. There were many inflammatory cells. Several small aggregations of epithelial cells were found in the granulation tissue (perhaps entrapped normal epithelial cells). Further tissue study was recommended.

The one patient who had a positive smear with the biopsy reported as indeterminate had a known case of carcinoma of the cervix with distant metastases, had received radiation therapy elsewhere, and had entered this hospital for biopsy of a suspicious lesion on the cervix. The pathologist reported that the tissue received was inadequate for diagnosis.

SUMMARY AND CONCLUSIONS

A group of 2,059 patients were screened for the cytological detection of carcinoma of the cervix uteri by means of the Draghi detection tampon. Of these, 758 patients had the tampon left in the vagina overnight, while 1,301 patients had the tampon in the vagina for a shorter period of time (10 to 45 minutes). Some problems were encountered due to lack of knowledge on the part of the patients in the use of the tampon. It has become apparent, however, in those patients who are returning now for their regular six month pelvic examination and in those patients who have reported for examination in the tumor clinic every two months, that, after instructions were given the first time the detection tampon was used, it was not necessary to repeat the instructions. In the 147 patients screened by the use of the detection tampon who had dilation and curettage and/or biopsy of the cervix, there was correlation of the biopsy and the cytology in 90.5%. There was a discrepancy between the biopsy and the cytology in 9.5%, with negative cytology and a positive biopsy in 7.48%.

It would appear, from the above, that the use of the Draghi detection tampon is a satisfactory method for obtaining smears for the mass screening of patients for the cytological detection of carcinoma of the cervix uteri. In view of the fact that, in 7.48% of those patients in whom it was possible to compare the smear and a biopsy, there was a negative smear and a positive biopsy, it would seem advisable that several smears at relatively frequent intervals on the same individual might reduce this figure. The final diagnosis, however, must depend upon a thorough gynecologic examination and biopsy.

Sheep Cell Agglutinins.—The sheep cell agglutinins, or heterophile antibodies, which appear at some time in the course of most cases of infectious mononucleosis can be differentiated from the heterophile antibodies present in most normal sera by their failure to be absorbed out with guinea pig kidney. Since the latter is rich in Forssman antigen, it will remove the normal sheep cell agglutinin and leave the mononucleosis heterophile antibody. This absorption technique is useful in determining the significance of titers at the upper limit of normal in suspected cases. The upper limit of normal with unabsorbed sera with the usual techniques is in the neighborhood of 1:64-1:128. Here again, a definite augmentation of sheep cell titer during convalescence from clinical illness has far greater significance than a single determination. The differential sheep cell agglutination test is based on the observation that agglutination of sheep cells by anti-sheep-cell-rabbit serum, a simple antigen-antibody reaction, is greatly enhanced by a factor occurring in about 75 per cent of the patients with peripheral rheumatoid arthritis. Significant sensitized sheep cell titers are rarely encountered in any condition other than rheumatoid arthritis. There seems to be no close correlation with severity of rheumatoid arthritis and the titer is apparently unaffected by any form of therapy, including cortisone and ACTH. The exact nature of the agglutinating factor is still unsettled.—C. Howe, Evaluation of Diagnostic Tests in Infection, *Bulletin of The New York Academy of Medicine*, October, 1955.

LARGE DOSES OF ATROPINE

LOW TOXICITY AND EFFECTIVENESS IN ANTICHOLINESTERASE INTOXICATION

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The medical importance of anticholinesterase agents has become increasingly apparent in recent years, and organic phosphate compounds have been widely publicized as "G agents" or "nerve gases." Their potential use as chemical warfare agents against military or civilian populations makes it important that the medical profession become better acquainted with the diagnosis and treatment of anticholinesterase intoxication.[1] The organic phosphates are also among the most powerful and versatile insecticides developed to date, and extensive agricultural use has resulted in many accidental exposures and deaths. Cases of poisoning have occurred in workers and in adult and children nonworkers who have come into contact with these substances. Most cases reported in the literature have been due to ignorance or improper handling of the insecticide. The substantial number of severe cases brings organic phosphate poisoning into the province of all practitioners.

TREATMENT OF ANTICHOLINESTERASE POISONING

At the present time the best known treatment for organic phosphate poisoning consists of: (1) atropine sulfate to control the muscarinic and central nervous system effects; (2) artificial respiration to treat the respiratory failure; and (3) general supportive therapy for other symptoms. The therapeutic importance of atropine has been emphasized by controlled studies [2] and clinical experiences.[3] The recommended initial and maintenance doses appear massive when compared with the usual therapeutic dose of 0.4 to 0.6 mg. (1/150 to 1/100 grain).

Grob [4] has reported that in the presence of anticholinesterase agents, patients have a markedly increased tolerance for atropine. Military recommendations [5] are that, in cases of mild or moderate symptoms of poisoning, 2 mg. of atropine sulfate (1/30 grain) should be injected intramuscularly. However, this dose of atropine may be inadequate where massive exposures have occurred. If severe symptoms of organic phosphate poisoning are present, 4 to 6 mg. of atropine (1/15 to 1/10 grain) should be injected intravenously or, if this is not feasible, intramuscularly. Similar dosage recommendations are made if severe respiratory distress or convulsions constitute a portion of the clinical syndrome. After the initial dose, 2 mg. should be administered at hourly intervals or oftener until signs of atropinization appear or as long as muscarinic effects are present.[6] Most investigators make similar recommendations.[7] A survey of 149 cases of organic phosphate poisoning reported in the English literature, including 15 deaths, reveals that even larger amounts of atropine than were administered would have been beneficial. Although symptoms were well reported,[8] sufficient data for analysis of atropine therapy have been presented in only 25 of these cases, in 9 of which the patients died. These data are summarized in table 1. (One hundred ninety-eight cases reported by Abrams [3b] do not present sufficient data on symptoms or atropine therapy to be included in this analysis.)

In reviewing this material, several considerations must be kept in mind. First, the cases cannot be compared with respect to degree of poisoning. No attempt has been made to separate cases on this basis, since the presentations are not complete enough to assay the severity of exposure. Secondly, the response to atropine therapy cannot be compared in all cases, since the exact times and amounts of injections have been incompletely detailed. Despite these limitations, several important differences are noted between the surviving and nonsurviving groups as regards atropine therapy. Table 1 reveals that the survivors received their initial atropine slightly later (141 minutes) than the nonsurvivors (113 minutes). However, exclusion of two patients with atypical cases (5 and 17), one of whom received his atropine within 7 minutes and the other at the end of 16 hours, makes the groups more homogeneous; the time of first atropine injection then becomes 82 minutes for survivors and 126 minutes for nonsurvivors.

The mean initial dose given each group was essentially the same. Analysis of individual cases reveals that only 3 of the 25 patients received an initial dose of at least 2 mg. These three were in the group of survivors. At the end of five hours of treatment, 7 of the 16 survivors (or 44%) had received 2 mg. or more of atropine, whereas, of the 7 nonsurvivors still alive at this time, only one (or 14%) had received this amount of the drug. Comparison of therapy beyond this point is impossible, since all of the nonsurvivors had died within 10 hours except two, one of whom lived 12 hours and the other 13.5 hours. The most important observation here is that in most instances neither the survivors nor the nonsurvivors were considered severely enough poisoned to require the recommended initial or maintenance dose of 2 mg. of atropine. Recent studies and experiences,[3] as well as this survey, further stress the necessity for speed and this large initial and maintenance dose. The survivors usually received their atropine sooner, and received more of it during the first few hours, but survival in some of these cases may have been due to less severe exposure.

The small doses of atropine usually administered indicate that: (1) initial intoxication was not considered severe enough to warrant large doses of the drug; or (2)

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toxic effects were feared from large doses of atropine. This latter factor is probably important because of the clinical habit of administering smaller doses. Accordingly, we have reviewed the literature on atropine in order to assay the toxicity of this drug, especially in large doses.

REVIEW OF LITERATURE ON ATROPINE INTOXICATION

The minimal lethal dose of atropine has been reported as 10 to 20 mg. in children and 80 to 130 mg. in adults.[9] Thus there is a wide margin of safety between effective and lethal dose. In adults who are sensitive to the drug, 5 to 10 mg. may produce a rather severe intoxication, with a rapid heart rate, dry mouth, pupillary dilatation, and central effects such as restlessness, confusion, and even mania.[9c] Since the middle of the 19th century, many cases of ingestion of large doses of atropine and atropine poisoning have been reported. These two are not synonymous, since cases of poisoning occur with relatively small doses and must represent a sensitivity to the drug.[9b] Recent studies in this laboratory indicate that atropine-induced orthostatic hypotension may serve as a useful measure of such individual sensitivity.[10]

Cases of atropine intoxication fall into three general categories: Those resulting from (1) large doses given for experimental purposes; (2) large doses given for specific therapeutic reasons; and (3) large doses not administered for experimental or therapeutic purposes, such as suicidal attempts, hypersensitivity, and accidental ingestion. The use of atropine for experimental purposes is usually limited to doses of 1 to 10 mg. In this laboratory, over 400 normal adult male students and military personnel have been given intramuscular injections of 2 mg. of atropine sulfate without any serious effects.[10] The most common symptoms were found to be dryness of the mouth, lips, and throat; tiredness; dizziness; headache; and tachycardia. Visual disturbances, flushing, and dysuria were also noted, but none of the symptoms were incapacitating, and all of the subjects returned to routine work at the completion of the tests. Robinson [11] has reported extensive studies on normal student and military volunteers with use of up to 3 mg. of atropine. No serious effects were noted other than tachycardia and limitation of work at warm temperatures because of impaired heat regulation. Other articles in the literature that report the experimental use of atropine [12] reveal over 250 persons who have participated, with no deaths or serious effects.

The actual dose of atropine taken in accidental exposures usually cannot be ascertained. Where atropine has been taken orally [13] or by hypodermic [14] the dose can be estimated, but when the atropine has been absorbed through the eyes,[15] from dressings and plasters,[16] or as a result of eating plants or animals containing the alkaloid,[17] the amount absorbed cannot be estimated. A

TABLE 1.—*Summary of Atropine Treatment for Anticholinesterase Poisoning* *

Case No.	Age, Yr.	Sex	Onset of Symptoms After Known Exposure or Last Possible Exposure	Initial Dose: Mg.	Initial Dose: Minutes After Onset of Symptoms	Atropine Therapy †: Cumulative Dose, Mg. (Hr. After Onset of Symptoms): 1	2	3	4	5	10	24	Total Dose, Mg.	Time of Death After Onset of Symptoms, Min.‡	Reference
1	Adult	F	Immediate	0.65	30	0.65	0.65	1.3	1.9	5.2	10		10		8e
2	Adult	M	Immediate	0.48	120	0	0	0.48	.48	0.48	1.7	3.9	4.7		8e
3	Adult	M	Immediate	0.65	30	0.65	0.65	1.3	2.2	2.6	3.2	3.2	3.2		8e
4	19	M	Immediate	0.48	50	0	0.48	0.48	0.48	0.48	0.48	0.48	0.48		8e
5	18	M	Immediate	0.86	960	0	0	0	0	0	0	2.0	2.5		8e
6	24	M	Immediate	0.65	90	0	0.65	0.65	1.3	1.3	3.2	3.7	3.7		8e
7	18	M	60 min.	0.65	105	0	0.65	0.65	1.3	1.3	3.2	3.7	3.7		8e
8§	5 mo.	M	.....	1.9	60	0	1.9	1.9	2.7	2.7	3.5	6.3	13.1		8b
9§	2	M	60 min.	2.1	60	0	2.1	2.1	2.1	2.1	2.1	5.9	5.9		8i
10	50	M	.....	0.48	..	....	....	....	....	....	....	6.4	6.4		8m
11	..	M	Immediate	0.64	150	....	....	....	....	....	....	1.3	1.3		8m
12	..	F	.....	0.96	40	....	....	....	....	....	....	2.9	3.8		8m
13	46	M	345 min.	1.1	75	0	2.0	2.6	3.3	3.9	4.6	7.1	7.1		8k
14	24	M	90 min.	0.65	90	0	.65	1.8	2.5	3.3	3.8	4.4	17.4		8a
15	18	M	Immediate	0.65	30	0.65	.65	0.65	0.65	.65	.65	0.65	0.65		8a
16	19	M	Immediate	2.6	180	0	0	0	2.6	3.9	11.0	11.0	24.0		8e
Mean				0.96	141‖ 82¶										
17	16	M	Immediate	0.86	7	0.86								7	8e
18	35	M	30 min.	0.65	130	0	0	2.6	2.6	3.2	3.2			600	3c
19	Adult	M	480 min.	0.65	450	0	0	0	0	0	0.65			810	8e
20	Adult	M	Immediate	0.86	90	0	0.87	0.87	0.87	0.87				480	8e
21	26	M	Immediate	0.65	105	0	0.65	0.65	0.65	0.65				420	8e
22§	2	F	.....	0.96	60	0	0.96	0.96	0.96	0.96	0.96			750	8b
23§	9 mo.	F	60 min.	1.6	40	1.6	1.6	4.8						180	8i
24	18	M	Immediate	0.48	120	0	0	0.48	0.96	1.4	2.7			570	8a
25	..	M	Immediate	0.65	15	0.65	0.65	0.65	0.65	0.65				335	8a
Mean				0.82	113‖ 126¶										

* Cases tabulated are only 25 in which specific dosage of atropine is reported out of 149 in literature. Parathion was the agent used in all cases except case 17, in which tetraethylpyrophosphate was used.
† Dosage reported exactly or approximately; ..., dose unknown; 0, no dose given; blank space, died.
‡ Patients in cases 1 through 16 recovered.
§ Children's dosage reported as adult equivalent on a milligram per kilogram basis.
‖ Mean of all cases.
¶ Cases 5 and 17 excluded from mean as atypical.

review of 110 cases of accidental intoxication reveals only nine deaths, which are considered in detail later.

In 272 cases of multiple large doses of atropine given for therapeutic reasons, only two deaths resulted.[18] Most of these patients had Parkinsonism or mental disease. The most common signs and symptoms noted were dryness of the skin and mucous membranes, increased pulse and respiratory rate, impaired vision and dilated pupils, excitement, dizziness, and hallucinations. Hyperthemia, hypertension, flushing, confusion, ataxia, and urinary frequency were also noted occasionally. These data on multiple doses of atropine, strictly speaking, are not completely comparable to those on single large doses, since it has been shown that repeated use, such as in Parkinsonism, results in increased tolerance to the drug.[19]

This over-all survey includes almost 1,000 people who have received atropine in excess of the usual therapeutic maximum of 1 mg. Most have received 2 mg. or more, and about one-third have received more than 10 mg. One patient survived an oral dose of 1,000 mg.[13a] These cases represent a total of between 4,000 and 5,000 individual doses of atropine. Eleven persons have died, and these cases are analyzed individually in table 2. From this table it can be seen that the patients in cases 2, 4, 5, and 7 were in poor physical condition, which may have contributed to their death. In case 1, the author states he was not sure that atropine had caused the death, although no other diagnoses are offered. The patient in case 8 had 1.5 grains (90 mg.) of morphine prior to death, which was believed to be from respiratory failure.

In three other cases (7, 10, and 11) there were also contributing factors. Case 7 represents an instance of chronic belladonna poisoning over a period of six years and cannot be compared with the remainder of the cases, which represent acute poisoning. Case 10 represents a statement by Arnold that he had known death to occur in five minutes from 1/30 grain (2 mg.) of atropine given by hypodermic. The five minute time of death is far out of range of the other deaths, and it would appear that some factor other than just extreme atropine sensitivity was responsible. In case 11, the 3½-year-old child received 1.35 gm. of phenobarbital at the same time that 540 mg. of extract of belladonna was ingested. In cases 3, 6, and 9 there is no evidence of factors other than atropine contributing to death of the patients. It is interesting to note that in five of the deaths respiratory failure was involved. This raises the question of whether efficiently administered artificial respiration and oxygen therapy might have benefited these patients. Almost half of the deaths occurred following ocular administration, and over 50% were in infants and children. This emphasizes the greater sensitivity in the young and by application to the eyes.

A detailed discussion of the diagnosis and treatment of atropine poisoning is outside the realm of this paper. Diagnosis can usually be established on the basis of history, physical findings, and use of the diagnostic test of Dameshek and Feinsilver.[20] Treatment is symptomatic, although benefits have been reported from the use of physostigmine or pilocarpine.[21]

COMMENT

This survey reemphasizes the necessity for large doses of atropine in the treatment of anticholinesterase intoxication. Review of reported cases of poisoning by these chemical warfare and insecticide agents reveals a direct relationship between survival, the amount of atropine given, and the speed of administration. It also stresses the minimal hazard from the recommended dose of 2 mg., which appears large by comparison with the usual clinical dose. The consequences of inadequate treatment for anticholinesterase intoxication are grave, whereas the effects of excessive administration of atropine, although uncomfortable and occasionally temporarily incapacitating, are not serious. Accordingly, treatment should tend toward overatropinization rather than underatropinization. This becomes even more important in view of the finding that there is a marked tolerance for atropine in the presence of anticholinesterase poisoning.

TABLE 2.—*Summary of Atropine Deaths Reported in Literature*

Case No.	Age, Yr.	Route of Administration	Dose,* Mg.	Time of Death, Hr.	Comment	Reference
1	1	Eyes	...	12.5	Author doubtful as to cause of death	15m
2	1	Eyes	...	13	Sickly, delicate child, subject to convulsions; author doubtful as to the cause of death	15l
3	2¾	Eyes	1.6	48	.....	15c
4	3	Eyes	18.1	20	Perforated cornea; died after surgery	9b
5	3	Eyes	...	15	Patent ductus arteriosus; poor physical condition	9b
6	9	Oral	...	48	Child ate deadly nightshade berries	17a
7	32	Oral	...	6 yr.	Chronic poisoning, belladonna tincture 2 drams (8 cc.) daily, 6 yr.	18d
8	43	Oral	198	15	Treatment included 1.5 grains (0.1 gm.) of morphine	13b
9	53	Hypodermic	32	115	.....	11b
10	..	Hypodermic	2	5 min.	From old literature, questionable	14b
11	3½	Oral	540	33	Simultaneous ingestion of 1.35 gm. of phenobarbital	13m

* Adult equivalent doses are used and figured on a milligram per kilogram basis.

Atropinization must be rapidly instituted and vigorously pursued according to the schedule recommended above. The failure of appearance of signs of atropinization after a 2 mg. dose of the drug offers further presumptive evidence of intoxication by an anticholinesterase. Patients with moderately severe symptoms may require large amounts of the drug before evidences of atropinization appear. The effects of atropine are somewhat prolonged, lasting 3 to 5 hours after one or two injections and 12 to 24 hours after overatropinization. The usual signs of overatropinization include drowsiness, restlessness, slowing of motor activity; dryness of mouth and mucous membranes; dry, flushed skin; tachycardia; pupillary dilatation; and urinary retention. With larger doses these are accentuated, and there may be disorientation, hallucinations, and even maniacal behavior. Some of these may be difficult to differentiate in the presence of signs of organic phosphate poisoning. The three signs that appear most reliable in differentiating the onset of

atropinization are (1) pupillary dilatation, (2) decreased or absent salivation and mucous membrane secretions, and (3) dryness of the skin.

In addition to the use of atropine, the treatment of organic phosphate poisoning includes: application of a gas mask and/or removal from the site of the vapors; immediate washing away of any liquid contamination; aspiration or drainage of excessive bronchial secretions that may be obstructing the airway; manual or mechanical artificial respiration, if necessary; oxygen, if necessary and available; ocular instillation of 2% homatropine or 0.5 to 1% atropine to counteract eye symptoms produced by the local absorption of organic phosphate agents; and anticonvulsant medication if convulsions are not controlled by atropine and are endangering the patient's life. Effects of anticholinesterase agents are prolonged, since recovery depends mainly on regeneration of cholinesterase enzyme in tissues. Treatment must be continued vigilantly until evidences of intoxication are no longer present. Severe exposure or delayed therapy may result in paralysis of respiration and death in spite of efforts to save the patient. Prompt masking and treatment significantly increase the chances of survival. If recovery occurs it will be complete, unless anoxia or convulsions were severe or prolonged enough to result in irreversible central nervous system damage.

1853 W. Polk St. (12) (Dr. Gordon).

1956 REVISIONS OF STANDARD BIRTH AND DEATH CERTIFICATES

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Every one of us, no matter how small or large his impress on the world, will leave behind two permanent records. These are his birth and death certificates. Curiously enough, it is the medical profession, which finds all paper work out of character, that is largely responsible for the creation and quality of these two records. And the records, in turn, serve as a history of the impact of medicine on the lives of the people. In this country the legal authority for registration rests with the governments of the 48 states. National birth and death data become possible because a standard record form is developed by the Public Health Service in cooperation with the state registration officials and representatives of health and demographic interests. The first standard certificates were promulgated in 1900, and the sixth will be used beginning Jan. 1, 1956. Most state registration offices have adapted the standard forms to their local needs but have retained the items needed for national statistical tabulations.

The basic information collected on birth and death certificates has not changed very much in the half-century of their use. Proposals for the collection of additional information are screened rigorously in the process of the decennial revisions, and only those of broad general value survive to become part of the legal document. The changes made in the 1956 revisions were designed to keep the certificates up-to-date and the collection of information accurate rather than to introduce any real innovations.

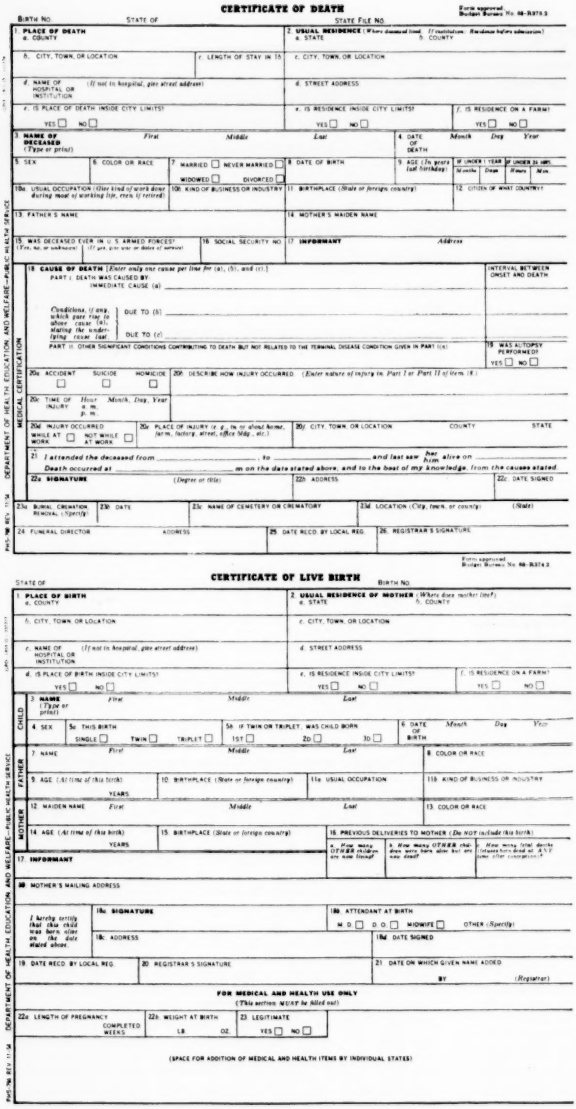
One of the current changes is a reflection of the increased urbanity of our population. A traditional statistic compiled from birth and death certificates has been birth and death rates for the city and the rural populations. Everyone "knows" that birth rates are higher for rural residents than they are for city people and that death rates are higher for the cities than they are for the rural areas. But the vital statistician attempting to compute birth and death rates for the urban and rural populations finds himself frustrated, because it is not possible to identify positively the city dweller. The addresses of suburbanites, living outside the city limits, often carry a city postal zone number and the city name. These persons are mistaken for city residents, and consequently vital events for city residents are overstated and those for rural residents understated. As the suburban population has increased, errors of this nature have also grown. On the 1956 certificates, the method of asking for information as to the place of occurrence and of residence has been revised to ensure better specification of urban residence and to clearly separate the truly rural or farm population (fig. 1). The farm residence question is a simple one, requiring no special definitions of farm. The informant is asked to follow the common understanding of what a farm is in answering the question. While in a few marginal cases people may differ in their interpretation of the word farm, in most areas of the country no problem is expected to arise.

Chief, National Office of Vital Statistics, Public Health Service, Department of Health, Education, and Welfare.

DEATH CERTIFICATE

On the death certificate the medical certification section has been revised slightly. The principle of reporting a sequence of causes that led to death, reporting the underlying cause last, is the same, but the instructions shown on the certificate have been simplified, since the medical profession is now familiar with the reporting procedure. The items requesting date of operation and major findings of operation have been deleted, because significant findings of operations are correctly reported in the cause-of-death sequence or as contributory causes. As may be seen from the certificate, the medical certification is in two parts. Part 1 relates to the sequence of events that led to death. In part 2 are to be entered any other significant conditions that unfavorably influenced the course of the morbid process and thus contributed to the death but that were not related to the disease or condition directly causing death.

On line (*a*) in part 1 is to be reported the immediate cause of death. Symptoms or modes of death, such as respiratory failure, heart failure, or collapse, are to be avoided. On lines (*b*) and (*c*) are to be reported the antecedent conditions that gave rise to the cause stated



CERTIFICATE OF DEATH

Form approved. Budget Bureau No. 68-R370.3

BIRTH NO. STATE OF STATE FILE NO.

1. PLACE OF DEATH a. COUNTY b. CITY, TOWN, OR LOCATION c. LENGTH OF STAY IN 15 d. NAME OF HOSPITAL OR INSTITUTION (If not in hospital, give street address) e. IS PLACE OF DEATH INSIDE CITY LIMITS? YES NO

2. USUAL RESIDENCE (Where deceased lived. If institution, Residence before admission) a. STATE b. COUNTY c. CITY, TOWN, OR LOCATION d. STREET ADDRESS e. IS RESIDENCE INSIDE CITY LIMITS? f. IS RESIDENCE ON A FARM?

3. NAME OF DECEASED (Type or print) First Middle Last

4. DATE OF DEATH Month Day Year

5. SEX 6. COLOR OR RACE 7. MARRIED NEVER MARRIED WIDOWED DIVORCED 8. DATE OF BIRTH 9. AGE (In years last birthday) IF UNDER 1 YEAR Months Days IF UNDER 24 HRS. Hours Min.

10a. USUAL OCCUPATION (Give kind of work done during most of working life, even if retired) 10b. KIND OF BUSINESS OR INDUSTRY 11. BIRTHPLACE (State or foreign country) 12. CITIZEN OF WHAT COUNTRY?

13. FATHER'S NAME 14. MOTHER'S MAIDEN NAME

15. WAS DECEASED EVER IN U. S. ARMED FORCES? (Yes, no, or unknown) (If yes, give war or dates of service) 16. SOCIAL SECURITY NO. 17. INFORMANT Address

MEDICAL CERTIFICATION

18. CAUSE OF DEATH [Enter only one cause per line for (a), (b), and (c).]
PART I. DEATH WAS CAUSED BY: IMMEDIATE CAUSE (a)
Conditions, if any, which gave rise to above cause (a), stating the underlying cause last. DUE TO (b) DUE TO (c)
PART II. OTHER SIGNIFICANT CONDITIONS CONTRIBUTING TO DEATH BUT NOT RELATED TO THE TERMINAL DISEASE CONDITION GIVEN IN PART I (c)
INTERVAL BETWEEN ONSET AND DEATH
19. WAS AUTOPSY PERFORMED? YES NO

20a. ACCIDENT SUICIDE HOMICIDE 20b. DESCRIBE HOW INJURY OCCURRED. (Enter nature of injury in Part I or Part II of item 18.)
20c. TIME OF INJURY Hour a.m. p.m. Month, Day, Year
20d. INJURY OCCURRED WHILE AT WORK NOT WHILE AT WORK 20e. PLACE OF INJURY (e. g., in or about home, farm, factory, street, office bldg., etc.) 20f. CITY, TOWN, OR LOCATION COUNTY STATE

21. I attended the deceased from ____ to ____ and last saw him/her alive on ____. Death occurred at ____ on the date stated above, and to the best of my knowledge, from the causes stated.
22a. SIGNATURE (Degree or title) 22b. ADDRESS 22c. DATE SIGNED

23a. BURIAL, CREMATION, REMOVAL (Specify) 23b. DATE 23c. NAME OF CEMETERY OR CREMATORY 23d. LOCATION (City, town, or county) (State)

24. FUNERAL DIRECTOR ADDRESS 25. DATE RECD. BY LOCAL REG. 26. REGISTRAR'S SIGNATURE

PHS-706 REV. 11-54 DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—PUBLIC HEALTH SERVICE

Form approved. Budget Bureau No. 68-R370.2

CERTIFICATE OF LIVE BIRTH

STATE OF BIRTH NO.

CHILD

1. PLACE OF BIRTH a. COUNTY b. CITY, TOWN, OR LOCATION c. NAME OF HOSPITAL OR INSTITUTION (If not in hospital, give street address) d. IS PLACE OF BIRTH INSIDE CITY LIMITS? YES NO

2. USUAL RESIDENCE OF MOTHER (Where does mother live?) a. STATE b. COUNTY c. CITY, TOWN, OR LOCATION d. STREET ADDRESS e. IS RESIDENCE INSIDE CITY LIMITS? YES NO f. IS RESIDENCE ON A FARM? YES NO

3. NAME (Type or print) First Middle Last

4. SEX 5a. THIS BIRTH SINGLE TWIN TRIPLET 5b. IF TWIN OR TRIPLET, WAS CHILD BORN 1ST 2D 3D 6. DATE OF BIRTH Month Day Year

FATHER

7. NAME First Middle Last 8. COLOR OR RACE 9. AGE (At time of this birth) YEARS 10. BIRTHPLACE (State or foreign country) 11a. USUAL OCCUPATION 11b. KIND OF BUSINESS OR INDUSTRY

MOTHER

12. MAIDEN NAME First Middle Last 13. COLOR OR RACE 14. AGE (At time of this birth) YEARS 15. BIRTHPLACE (State or foreign country) 16. PREVIOUS DELIVERIES TO MOTHER (Do NOT include this birth) a. How many OTHER children are now living? b. How many OTHER (that is, born before this birth) children were born alive but are now dead? c. How many total births (other than this birth) did mother have?

17. INFORMANT

18. MOTHER'S MAILING ADDRESS

I hereby certify that this child was born alive on the date stated above.

18a. SIGNATURE 18b. ATTENDANT AT BIRTH M. D. D. O. MIDWIFE OTHER (Specify) 18c. ADDRESS 18d. DATE SIGNED

19. DATE RECD. BY LOCAL REG. 20. REGISTRAR'S SIGNATURE 21. DATE ON WHICH GIVEN NAME ADDED BY (Registrar)

FOR MEDICAL AND HEALTH USE ONLY (This section MUST be filled out)

22a. LENGTH OF PREGNANCY COMPLETED WEEKS 22b. WEIGHT AT BIRTH LB. OZ. 23. LEGITIMATE YES NO

(SPACE FOR ADDITION OF MEDICAL AND HEALTH ITEMS BY INDIVIDUAL STATES)

PHS-706 REV. 11-54 DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—PUBLIC HEALTH SERVICE

Fig. 1.—Examples of the 1956 revision of standard death and birth certificates.

in line (*a*), the underlying cause of death being stated last in the sequence of events. The underlying cause is defined as the cause that started the chain of events that led to death. If the disease or condition directly leading to death stated in line (*a*) described completely the train of events, it is not necessary to fill in lines (*b*) and (*c*). The cause of death used for routine statistical tabulations is the underlying cause of death. In effect, the physician has been asked to certify the causes of death in such a manner that he is the person to select the cause of death for the statistical tabulations. This procedure, which has been adopted internationally at the recommendation of the World Health Assembly, has resulted in statistics that reflect medical opinion more than they did in the past.

Even though the new procedure has been in effect for seven years, it is estimated that more than 20% of the death certificates are returned with the medical certification improperly completed; that is, the cause reported last was obviously not the cause the physician intended to designate as the underlying cause of death. Rather than permit these errors to be carried into the cause-of-death statistics, the World Health Organization has suggested general rules that serve to classify the inadequate certifications as if they had been reported in correct sequence. No rule, however, can result in statistics that are as reliable as those compiled from carefully and correctly reported data by the person who is in a better position than anyone else to determine the cause of death—the attending physician. It is realized that it is not always possible to make a precise diagnosis, but even in these cases the probable diagnosis, with appropriate qualifications, reported by the physician is the best information available concerning the cause of death. A few case histories abstracted from hospital records, together with the filled out medical certification form, may serve to illustrate the proper method of reporting causes of death.

CASE 1.—On Sept. 30, 1955, a 67-year-old female was admitted to the hospital with a strangulated femoral hernia that occurred three days prior to admission and that was causing abdominal pain and fecal vomitus. The second day after the hernia had become strangulated, there was perforation of the small intestine. On Oct. 1, the strangulated hernia was released and a resection of the intestine with end-to-end anastomosis was made. On Oct. 2, acute peritonitis set in, and the patient died on Oct. 13.

In this case, line (*a*), part 1, of the medical certificate would read acute peritonitis, line (*b*) perforation of small intestine, and line (*c*) strangulated femoral hernia, with interval between onset and death being 11 days for (*a*), 14 days for (*b*), and 16 days for (*c*).

CASE 2.—On Feb. 14, 1955, a 76-year-old male slipped and fell on the ice while cleaning church steps. He was admitted to the hospital, where fractures of the left ischium and ilium were reduced. Examination showed azotemia, general arteriosclerosis, arteriosclerotic heart disease, and pulmonary emphysema. He developed bronchopneumonia on Feb. 15 and died on Feb. 21. The findings at autopsy included fractured hip and pelvis, bronchopneumonia, cardiac hypertrophy, chronic fibrous myocarditis, and coronary sclerosis. An example of the manner in which the medical certificate should be filled out is given in figure 2.

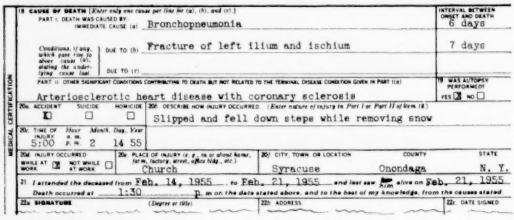

19 CAUSE OF DEATH
PART I: DEATH WAS CAUSED BY:
IMMEDIATE CAUSE (a) Bronchopneumonia
INTERVAL BETWEEN ONSET AND DEATH
6 days
Conditions, if any, which gave rise to (a), stating the underlying cause last
DUE TO (b) Fracture of left ilium and ischium
7 days
DUE TO (c)
PART II: OTHER SIGNIFICANT CONDITIONS CONTRIBUTING TO DEATH BUT NOT RELATED TO THE TERMINAL DISEASE CONDITION GIVEN IN PART I(a)
Arteriosclerotic heart disease with coronary sclerosis
19 WAS AUTOPSY PERFORMED? YES NO
MEDICAL CERTIFICATION
20a ACCIDENT SUICIDE HOMICIDE
20b DESCRIBE HOW INJURY OCCURRED (Enter nature of injury in Part I or Part II of Item 19)
Slipped and fell down steps while removing snow
20c TIME OF INJURY 5:00 P.M.
Hour 2
Month, Day, Year 14 55
20d INJURY OCCURRED WHILE AT WORK NOT WHILE AT WORK
20e PLACE OF INJURY (e.g., in or about home, farm, factory, street, office bldg., etc.)
Church
20f CITY, TOWN, OR LOCATION
Syracuse
COUNTY
Onondaga
STATE
N. Y.
21 I attended the deceased from Feb. 14, 1955 to Feb. 21, 1955 and last saw him alive on Feb. 21, 1955
Death occurred at 1:30 P.M. on the date stated above, and to the best of my knowledge, from the causes stated.
22a SIGNATURE (Degree or title)
22b ADDRESS
22c DATE SIGNED

Fig. 2.—Medical certificate for person who died of bronchopneumonia, showing the correct sequence of significant data reported.

CASE 3.—On Aug. 25, 1952, a 63-year-old male was admitted to the hospital where x-rays made on Aug. 31 showed adenocarcinoma of the rectum but no evidence of metastasis. Malignant neoplasm was removed on Sept. 13. A diagnosis of syphilis was also made. He was discharged on Nov. 3 as improved. On March 3, 1954, an x-ray examination at the dispensary showed pelvis apparently normal; however, there was an unusual shadow to the left of the sacrum. On June 19, he was readmitted with recurrent carcinoma of the rectum with invasion of the urinary bladder. He was discharged unimproved on July 27. On

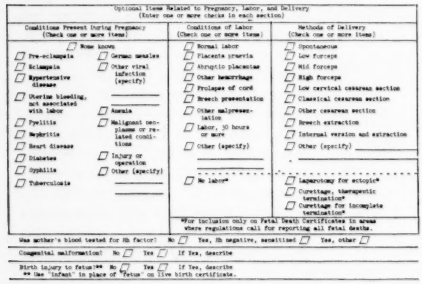


Fig. 3.—A supplemental medical and health section for live birth and fetal death certificates.

Jan. 3, 1955, he reported to the dispensary for treatment of the carcinoma of the rectum and was admitted to the hospital on Jan. 4. The examination showed a recurrent carcinoma of the rectum with invasion of the urinary bladder and metastases throughout the abdomen, syphilis, and decubitus ulcers. Bronchopneumonia developed on Jan. 9, and the patient died on Jan. 12. Autopsy confirmed the above findings.

The medical certificate would be filled out in the following manner: line (*a*), part 1, bronchopneumonia, line (*b*) metastatic cancer of bladder and abdomen, and line (*c*) adenocarcinoma of rectum, with interval between onset and death being (*a*) three days, (*b*) one year, and (*c*) three years. Part 2 would indicate syphilis as the other significant condition contributing to death.

BIRTH CERTIFICATE

A small change, designed to improve the usefulness of the statistics compiled from the item concerning children previously born to the mother, was made on the birth certificate. The responses to this item provide basic data for studies of fertility and an understanding of problems of fetal loss to mothers of differing ages and gravida. Item 16*c* (on the standard certificate) now requests information on all fetal deaths rather than just those of 20 weeks' gestation or more (fig. 1). The collection of this information, which has been endorsed by the World Health Organization, will make possible an important advance in the knowledge available on pregnancy wastage.

Many states now collect, in addition to the legally required information on the birth certificate, a supplemental medical and health section. This section is not part of the standard certificate and is frequently added at the bottom or on the back of the certificate. A checklist form for collecting the supplemental information has been successfully used in the state of New York, and an adaptation of that form (fig. 3) is recommended for use in other states planning special studies requiring this information.

Aldosterone.—There is a close correlation between aldosterone output and electrolyte balance in man. . . The effect of aldosterone may vary somewhat under various conditions of renal function, electrolyte load and capillary equilibrium. This is not surprising, since the effect of other corticosteroids is conditioned by physiologic factors. In normal man, aldosterone plays a part in renal adjustment to changes in electrolyte balance. This adaptation is impaired in primary adrenal insufficiency. Removal of the pituitary does not necessarily result in loss of this capacity; aldosterone output may be increased during sodium deprivation in a patient after hypophysectomy. In the adrenogenital syndrome and in Cushing's syndrome, the output of aldosterone is usually not far from normal. . . When excess aldosterone appears in a patient with heart disease, the nephrotic syndrome, hepatic cirrhosis or toxemia of pregnancy, the initial effect on the kidney is retention of sodium, and the accumulation of edema is favored by the disturbed capillary equilibrium. In this case, the high output of aldosterone is secondary to the presence of other diseases, and the effect of the hormone may be modified by changes in the kidneys and in other tissues. Aldosterone does not show its usual effects when the kidneys fail to respond. In a case of "sodium-losing nephritis," a high output of aldosterone was associated with dehydration and a loss of sodium in the urine; later the output of aldosterone fell to normal when a very high sodium intake resulted in improved hydration, with very high daily excretion of sodium. Aldosterone is secreted by the human adrenal. At a physiologic level its chief effects are to decrease sodium excretion and to increase potassium excretion. The fraction which appears in an active form in urine has been measured in normal men and in various patients. The output of aldosterone in normal men is closely related to sodium and potassium intake and balance, and suggests an effort to return the altered balance toward normal. The pituitary appears to have little control over its secretion in man. Aldosterone output is increased: (1) in normal men on diets low in sodium or high in potassium; (2) in the nephrotic syndrome, congestive heart failure, hepatic cirrhosis, or toxemia of pregnancy during periods of exacerbation and accumulation of edema: effective treatment and improvement of the underlying condition result in reduced aldosterone output and diuresis; (3) in tumors of the adrenal cortex which secrete aldosterone.—J. A. Luetscher Jr. and R. H. Curtis, Aldosterone: Observations on the Regulation of Sodium and Potassium Balance, *Annals of Internal Medicine*, October, 1955.

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PRESENT STATUS OF PREVENTIVE PSYCHIATRY

OBITER DICTA

Francis J. Braceland, M.D., Sc.D., Hartford, Conn.

An obiter dictum is, in the language of the law, an incidental or collateral opinion uttered by a judge and, therefore (as not material to his decision or judgment), not binding. Should such opinions be uttered by a lesser luminary, there is always the danger that the opinions will simply be considered individual impertinences, but in spite of this I propose that this present address of the Chairman of the Section on Nervous and Mental Diseases be considered as obiter dicta and certainly in no manner be held binding. The chairman of any section by reason of his position is supposed to have spent at least some little time on the Mt. Olympus of his particular specialty and, though his status is in no way juridical, it is not altogether unusual to expect that he will set forth some rather definite pronouncements that by custom and by courtesy no one in the audience will challenge. It is known that the chairman's Jehovah titer might be slightly elevated, even though his appreciation of the passage of time might be slightly depressed. The often hapless audience, more captive than captivated as Alan Gregg puts it, can only hope and pray that his terminal facilities are not altogether out of order.

PRESENT CONCEPTS OF MENTAL HEALTH AND DISEASE

This is a particularly propitious time to address the members of this section, for it is safe to say that today there is no subject within the entire field of medicine that is more widely and continually discussed than is psychiatry. This is true partly because of the urgency and the poignancy of man's personal problems in this present nuclear culture and partly because our present civilization looks upon man himself as a problem. Added to this, the whole field of psychiatry is presently in a ferment. New drugs have appeared that are obviously potent and in some fashion useful, and these drugs, in addition to helping the patients, are also "treating" the doctors. After a long arid period with an intervening short wave of adrenal enthusiasm, attention has now centered upon drugs that affect mood and influence behavior, and fields that long lay fallow are sown now with reserpine and chlorpromazine.

In addition to all of this, it is now becoming evident that medicine at midcentury is drifting more toward a unitary concept of health and disease, in which the patient is viewed not only in the light of pure science but also against the backdrop of his environment and as a contributor to his illness as well as its subject and object. This delights the psychiatrist. Health and disease are now being seen as modalities of life determined by forces and stresses arising from within and without the organism. This orientation, by no means new to medicine, was lost sight of when medicine became wholly absorbed in the scientific delineation of disease entities and assiduously tracked down their specific causes and cures. The whole unitary concept is now being rediscovered. Actually Claude Bernard (1813-1878) clearly indicated that health and disease are phases of life processes. He submitted that the conditions necessary to life are found neither in the organism nor in the outer environment but in both at once. The outer environment is essentially the same, he pointed out, for both living and inorganic forms, but the inner environment is special to each living being. The capacity to maintain internal homeostasis in the face of internal and external stress is therefore essential to health and to life. Thus, Claude Bernard laid the groundwork for an understanding of the dynamic properties of environment, internal and external, and the types of processes to be observed among them. The psychiatrist arrived laboriously and circuitously at the same understanding through his work with the emotionally sick.

Thirdly, the time is also propitious for addressing such a group because the whole amorphous field of mental health, hitherto marked by either complete neglect or wide diffusion of effort, has finally attracted the attention of the public at large and, in some instances, their legislative representatives, with the result that the magnitude of the problem is being recognized and various groups are casting about to see what can be done about it. Mental health week this year witnessed a gigantic cooperative effort in public education involving the use of all possible mediums of communication and reaching millions of people from coast to coast. What the results of this will be remains to be seen. That mass education will finally erase or correct certain conceptions and ideas that hamper progress in psychiatry is a happening devoutly to be wished for. Still prevalent, however, is the belief—a compound of truth and fallacy—that mental disorder comes from weakness of character, heredity, or way of life, together with the notion that cure of a psychotic break is a rarity.

Lest we be tempted to preen ourselves on our present-day advances, however, we should bear in mind that stigmatization is still the lot of the patient who is placed in a mental hospital even in these enlightened times. Laws regarding hospitalization, commitment, and financial support are antiquated. Hospitalization plans are openly discriminatory, some going so far as to deprive a patient of benefits should he be moved from the medical to the psychiatric ward of the same general hospital! People still have curious impressions of mental disease, even those who purportedly should know better. The tendency is not to consider as mentally ill a patient who shows no bizarre or violent behavior, even though he be suffering from a condition that if untreated leads to a disabling chronic condition, suicide, or worse. Obviously, therefore, there is still much work to be done.

Psychiatrist-in-Chief, Institute of Living.

Chairman's address, read before the Section on Nervous and Mental Diseases at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

AREAS FOR IMMEDIATE ENDEAVOR

Before embarking further on a discussion of the status of preventive psychiatry, which is the main concern of this presentation, I might perhaps anticipate a bit and, with no regard for orderly procedure, suggest what my conclusions regarding it will be. Admittedly preventive psychiatry, which is everybody's business, should be a very important concern of the discipline of psychiatry itself, but we are not yet equipped to understand which direction our efforts in this regard should take. To prevent something, we need to know its causation, and there is no need to say that we have not yet reached this happy state in regard to the several important psychiatric illnesses.

In the meantime, however, there are two segments of our problem that require our immediate and concentrated attention and involve things that we can do something about. The first is the improvement of our treatment procedures for the benefit of those patients who are presently ill in our hospitals. It is true that great strides in the proper direction have already been made in this regard and our hopes for assistance from drugs and chemical agents are much greater now than they have been for several decades. Caution is the watchword, however. These new therapeutic agents will have to be checked carefully and thoroughly before our enthusiasm about them beclouds our scientific vision. It does appear as though these drugs are potent additions to our armamentarium. They do control behavior in many instances, and they do help to control anxiety and agitation, but several years will be required before we can present a true evaluation of their efficacy. It behooves us all, therefore, to exercise restraint and to keep careful watch and careful records. It may be we are in the way of accomplishing great things in our new directions, but until we are sure we must restrain our enthusiasm, and particularly must we avoid being led to make statements that may ricochet upon the specialty, harm the patients, and disappoint families.

The second area that demands our attention is in the field of research. Funds are finally becoming available in increasing amounts for specific research projects. The problem now is to find capable personnel and research scientists to undertake the important work that is at hand. Already it is being hinted that there are more stipends available than there are satisfactory projects being presented or capable men to do the work. Unfortunately, it is not to be expected that these psychiatric research men will spring fully armed as did Athene from the brow of Zeus. In addition to the long years of training required of them and the meager pecuniary rewards that await them, they are now faced with a tour of two years of military service. True enough, the rewards of a researcher are scientific and spiritual and not to be measured in terms of cash, but these bright young men, many of them with families, are beset externally by the strong pull and the siren song of the lucrative private practice that their colleagues enjoy. It is only a consuming interest and a sense of dedication that will keep them from being lured from the fastness of their laboratories, and we must help in some fashion to keep these men at work. Obviously, this situation is a serious and pressing one. Without being melodramatic about it, we may say that the welfare of millions of sick people is dependent upon them. With funds available, interest high, and the crying need for excursions into unexplored scientific psychiatric areas, it would indeed be a tragic setback if we were to have to confess our inability to meet the demands made upon us because the laborers are few. Surely this problem is worthy of the sustained interest of all members of the specialty.

METHODS OF EFFECTIVE PUBLIC EDUCATION

To return to the question of prevention, "Satus est initius mederi quam fini" (It is better to doctor at the beginning than at the end.), from the "Adagia" of Erasmus, still holds. The question is how do we set about this part of our task. Education and the spreading of proper information is necessarily the first step to be taken, but it has been found in psychiatry, as it has to some extent in any field dealing with illness, that public information on what constitutes illness and health is a hodgepodge of folklore, information, and misinformation. As we have seen repeatedly, the use of mass propaganda methods may give a distorted picture of any public health problem. Certain hazards are involved as well. One of the hazards of any health campaign is the ease with which fears and anxieties are aroused in many people. Certainly the anxiety potential inherent in the thought of a mind's becoming diseased is paralleled only by that associated with the inevitability of death.

In a recent study of attitudes toward mental illness, Cumming and Cumming [1] investigated the results of an intensive educational program containing a wide variety of material. Working with two small homogenous communities in Canada, one experimental, the other control, and using before and after measurements, they found evidence of limited achievement in the teaching of sound principles and attitudes in the participating community. However, in the same community there was a suggestion of increasing anxieties, making for less adequate interpersonal relationships between the inhabitants. This points up the difficulties involved in changing attitudes toward mental health and disease. Public education regarding a terrifying illness tends to foster either emotional resistance or hypochondriacal preoccupation, and both reactions are destructive to prophylaxis. Our problem was heretofore to call attention to the ravages of mental illness. This mission has been accomplished, and we should now pursue a new approach. The theme of mental illness must always be placed in as favorable a light as is consistent with the facts and always from the point of view of the promise that research holds for the future. It is urgently important to stress the consideration that in most of the prevalent forms of mental illness, improvement or recovery is a common occurrence, particularly if early treatment is instituted. Psychiatrists and, in fact, all individuals who participate in psychiatric educational programs for the laity should endeavor to reassure rather than to threaten or frighten. They should, above all, make sure that they remain in the realm of fact rather

1. Cumming, M. E., and Cumming, J.: The Social Control of Mental Illness, with Special Reference to the Strategies of Isolation and Denial, to be published.

than soar to the stratosphere of theory or speculation where they are soon out of sight and hearing. It is axiomatic that the presentation should clarify rather than confuse and that the audience be spared technical language and abstruse, complex material that they are not prepared to handle.

Education in mental health should stress the wide range of normal behavior and the relativity of emotional well-being with its tendency to fluctuate from time to time, just as physical well-being tends to vary in every human being for reasons inherent or imposed. That emotions are a fundamental importance in human behavior and in both physical and mental health needs further amplification. The universality of anxiety, with its constructive as well as its destructive aspects and its somatic repercussions in addition to its psychological superstructure, is a basic point to get across. People need to understand that the past is a powerful determinant of the present, the unfailing reservoir of motivations and values, good and bad, important to the security of the individual. The impact of social and cultural factors on personality development and functioning is an important consideration in preventive psychiatry. A useful approach in preventive psychiatry is one that not only clarifies psychological needs at different periods of development but also indicates types of stress that lead to emotional insecurity and anxiety. Along with emphasis on the principles of child development and care and on problems of adolescence and maturity, marriage and parenthood, work and recreation, and aging and old age, there should be specific attention to the power of basic human emotions, especially the destructive ones that drive men violently forward to ephemeral goals and backward to immature behavior.

Probably mass methods of public education will always be less effective in reorienting the public to major social and public health problems than is the approach by small groups of key individuals in professions likely to influence popular opinion. Considerable interest and, often, particularly useful auxiliary work in mental health have emerged from such important groups as religious leaders, members of the legal profession, teachers and P. T. A. groups, public health nurses, community leaders, industrial supervisors, and trade union officials. These groups should be brought further into the orbit of preventive psychiatry and assigned additional responsibility in efforts to promote preventive and curative facilities and to secure support for basic research.

CAUSATIVE FACTORS AND PREVENTION

Prevention of mental illness is an exceedingly complex task. As already mentioned, it implies the control of causes. Unfortunately, in many important categories of psychiatric illness, the causes are not clearly established. We are quite certain, in fact, that with the exception of certain reactions clearly based on infection, organic disease, toxic states, and the like, though even here the picture is modified by the personality of the individual, no one cause operates in a reaction that we call psychiatric. Neither nature nor nurture affords a cogent explanation of neurosis or psychosis, though in cooperation with other factors each is undoubtedly significant. The multiplicity of possible causes would seem to make it difficult to know where to begin in the field of prevention. We know, however, that multiple causation does not preclude the possibility of effective therapeutic work. Clinical experience shows that an attack upon one or more of the various etiological possibilities in any given case may give symptomatic relief that is thoroughly worthwhile. The chain of psychopathology is sometimes no stronger than its weakest link, particularly if that link has been recently forged. So in prevention, we can work on some of the factors that we know tend to disturb the individual in his intrapersonal and interpersonal adjustment.

Sound programs of mental health are not limited to the provision of facilities for the diagnosis and treatment of malignant processes already under way. They involve attention to potential disturbances before they materialize, as well as to the danger signs of incipient mental disorders and to actual symptoms at an early stage. By giving immediate and long-term support, by administering first aid when necessary or by seeing that the patient gets it somewhere else, and by keeping in touch with patients discharged from psychiatric hospitals the mental health clinic can do much to prevent unnecessary admission and retention of patients in mental hospitals. The mental health clinic serves to bridge the enormous gap between the hospital and the community. Certainly money spent on child guidance and on classes for the education of the subnormal child is an excellent investment in public health. Certainly maternity and child welfare clinics offer substantial preventive opportunities; yet we should not forget that attention to our aging population would also yield enormous gains in prevention. The accumulation of experience shows more and more clearly that mental illness in patients over the age of 65 is often, in large part, a reactive condition and, therefore, preventable as well as treatable. As Holt [2] recently intimated in a survey of problems connected with the evaluation of mental health programs, a program designed to increase the quality of mental hygiene in older persons might have "as many beneficial effects in terms of the population generally as a program would that was designed specifically for its effect on children."

FAMILY PHYSICIAN'S ROLE IN PREVENTION

Current attempts to promote conditions favorable to mental health seem to be based on community projects drawing family and school experiences, employment resources, church, recreational outlets, and corrective and protective organizations into a broad program of mental health services.[3] One can have no quarrel with these efforts. At the same time, we should also note that the key preventive agent in the entire mental effort may well be the physician in community practice, for the physician in general practice sees every segment of the population, every age group, and persons at all economic and social levels. He is aware of the enormous suggestibility of patients in matters of health and of the mass of misin-

2. Holt, L. B.: Problems in the Evaluation of Mental Health Programs, in Witmer, H. L.: Evaluating the Approaches, Methods and Techniques for Developing Mental Health Programs, to be published.

3. Training and Research in State Mental Health Programs: A Report to the Governors' Conference, Chicago, the Council of State Governments, 1953.

formation that weighs upon them. False ideas absorbed from intimates, acquaintances, and reading of various kinds often propel them on a natural or unnatural journey toward anxiety and symptom formation. The family physician is in a strategic corrective position, and it is always an important part of his role to remove misapprehensions and to relieve anxiety in his patients.

It has been said that the best heredity in the world will not guarantee immunity from psychiatric disturbance if essential parts of the physical equipment have been damaged by accident or illness.[4] The practitioner plays a key role in the prevention of such tragedies. In his care of expectant mothers, in his obstetric work, in his care of babies and children, he may accomplish preventive psychiatry of heroic proportions. It is he who is in the best position to recognize and allay parental anxieties before these become disturbing to either the parents or the child. It is hoped that he will never forget that the time lapse for this to happen in is very short indeed; hence the advisability of dealing with tensions before and after the baby's birth and of handling parental concern during a child's illness and during other periods of stress. Helping parents with handicapped children is psychiatric prophylaxis of a high order. This help should be extended at the earliest possible moment, so that both child and family may be spared the harrowing emotional experiences that tend to arise in these tragic situations.

In his relationships with children, the family physician may be well able to neutralize the adverse effect of parental preoccupation with health. He can prevent unnecessary invalidism in children who, because of past illness, often completely overcome, are felt to be handicapped, delicate, or otherwise unfit for play and recreation. Hypochondriasis is easily engrafted on the immature personality, together with unhealthy preoccupation with the thinking and feeling self. Physicians know and others should learn that we should refrain from careless talk in the presence of a child, for a child is deeply concerned with his own body and is quick to pick up suggestions of direful possibilities. The doctor should be prepared to orient the child adequately for medical or surgical procedures; it is he who can best reassure his young patient, rather than the worried, overanxious parent. In treating patients in adolescence and early adulthood, the doctor should not neglect any opportunity he may have to correct false notions about health, particularly about tension-laden sexual questions. In the field of marriage guidance, he can do good preventive work by correcting certain common misapprehensions and so averting anxiety reactions that often arise at that time and not infrequently reach alarming proportions.

Thus, to the usual duties imposed upon the practitioner in the field of psychiatry; namely, the handling of the mildly sick or their referral to proper facilities and the early recognition and disposal of the more severe psychiatric disorders, is added the general preventive task of attempting to eliminate conditions in and about his patients that are generally harmful to mental health. In the introduction to his recent paper, "The Doctor, His Patient and the Illness," Balint [5] pointed out that by far the most frequently used drug in general practice is the doctor himself and that it is a drug without pharmacology, without directions as to dosage, form, and frequency of administration, and without leads to the hazards, allergic responses, or undesirable side-effects. We know, however, that it is an extremely powerful drug and that use of it relieves more suffering than has yet been recorded for the most powerful drug in the pharmacopeia. The family doctor of old knew this to be so and "prescribed" himself in generous doses. It is time that we recaptured his art, and, when we do, we will be mental hygienists par excellence, even if without portfolio.

200 Retreat Ave. (2).

4. Preston, G. H.: The Substance of Mental Health, New York, Farrar & Rinehart, 1943.

5. Balint, M.: The Doctor, His Patient, and the Illness, Lancet **1**: 683-688 (April 2) 1955.

CLINICAL NOTES

A SIMPLIFIED LIGHT-WEIGHT APPARATUS FOR KYMOGRAPHIC UTEROTUBAL INSUFFLATION

WITH AN EFFERVESCENT TABLET AS SOURCE OF CARBON DIOXIDE

Isidor C. Rubin, M.D., New York

The first kymographic uterotubal insufflation apparatus was assembled in 1925 and a report published in 1929.[1] Since then, a number of modifications have been devised by others. In general, the different types comprise a mechanism of precision essential for the scientific clinical determination of tubal patency and nonpatency, including various degrees of tubal obstruction, spasm, and subfunctional tubal conditions. By correlating pressures recorded on the kymograph with the calibers of graduated capillary tubes corresponding to the diameters of the human ovum, it has been possible to estimate degrees of tubal stenosis obstructive to passage of the ovum through strictured tubes.[2]

A discussion of modifications by others of the insufflation apparatus I assembled was given at Rio de Janeiro, Brazil, in 1949.[3] Without going into details, it appears that the different types of apparatus designed for uterotubal insufflation were based chiefly on claims of lighter weight, the use of aneroid manometers, or different flow meters and readier operability. These claims have some validity but by and large do not detract seriously from the serviceability of the Becker-

Because of space limitations figures 2 and 4 have been omitted from THE JOURNAL and will appear in the author's reprints.

The apparatus described was demonstrated at the International Congress of Obstetrics and Gynecology, Geneva, Switzerland, July, 1954, and is made by the Grafax Company, 32 E. 10th St., New York.

The effervescent tablets used in this study were supplied by the Ortho Pharmaceutical Corporation, Raritan, N. J.

The Swinney filter is made by Becton Dickinson & Company.

1. Rubin, I. C.: A New and Improved Apparatus for Uterotubal Insufflation, J. A. M. A. **92**: 1597 (May 11) 1929.

2. Rubin, I. C.: Tubal Obstruction as a Cause of Sterility and Its Nonoperative Treatment, Am. J. Obst. & Gynec. (supp.) **61A**: 698, 1951; Uterotubal Insufflation: Value in the Treatment of Tubal Obstruction to Ovular Migration, Fertil. & Steril. **5**: 311, 1954.

3. Rubin, I. C.: Physical and Dynamic Aspects of Kymographic Uterotubal Insufflation Including Apparatus, An. brasil. ginec. **28**: 329, 1949.

Rubin apparatus, which is sturdy, portable, and long-lasting. It has been used routinely in many cases since 1925 and continues to give complete satisfaction.

In terms of weight, most of the modified models are somewhat lighter. Whether they contain an electrically driven kymograph, an aneroid manometer, or a gas flow meter instead of a spring motor, a siphon meter, and a pressure reduction valve, respectively, makes little difference in the end-results. The important thing is that they contain the essentials for scientific determinations.

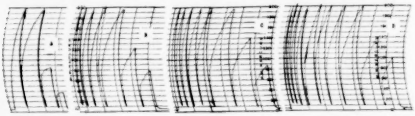

Fig. 1.—Duration of workable pressures produced by effervescence employable in uterotubal insufflation when (*A*) one-fourth, (*B*) one-half, (*C*) three-fourths, and (*D*) one whole tablet is used.

These essentials are realized in the Bonnet,[4] Sharman,[5] Kidde, Marbach,[6] Weisman,[7] and Grafax models and others. The compact Grafax insufflation apparatus was early devised to overcome the objection of size and weight. In this apparatus, a small siphon volumeter is combined with an aneroid manometer and a writing pen attached to a bellows, which was a distinct improvement. The spring motor was originally adopted to eliminate the noise caused by an electrically driven kymograph that interfered with auscultation for the tubal souffle. As silent electric motors have become available, one has since been adopted in the Grafax apparatus, which was made according to my specifications and has been found very useful and handy.

A drawback of practically all types of apparatus designed for scientific uterotubal insufflation is their initial cost. This has led to the adoption of so-called simplified methods, based on the use of air instead of carbon dioxide. Insufflation of air is fraught with danger of embolism, the disastrous effects of which are prevented by carbon dioxide insufflation. The safety of carbon dioxide has been amply and adequately established during the last 34 years, and it is the gas of choice, to which any type of insufflation apparatus is now adapted. However, in order to make the apparatus more generally available, it has been necessary to eliminate some of the costly parts. The reduction has been accomplished by means of a simple device.

COMPONENTS

For many years the writer has entertained the idea of using an effervescent tablet as source of supplying the carbon dioxide gas. This should eliminate a carbon dioxide tank and reduction valve and even the much lighter sparklet, which, however, requires a reserve chamber to take up its powerful pressure. The effervescent tablet does not require these parts because the entire volume of carbon dioxide needed for the Rubin test for patency of the fallopian tubes is contained in its component ingredients, which also necessarily determine the practical amounts of pressure. Preliminary experiments made with sodium bicarbonate and citric and tartaric acid combinations in powdered form and later in compressed tablets have yielded data as to the volume of carbon dioxide produced by different combinations of the ingredients, the duration of the effervescence, and the pressures recorded. The latter ranged from a certain maximum at full effervescence to zero, which was reached when the tablet was completely disintegrated. The actual amounts of carbon dioxide generated from the tablet compared roughly to the theoretical yield as calculated by chemical formulas. Tablets were found to be preferable to powders because they were dissolved more gradually, permitting better pressure control. Figure 1 demonstrates pressure curves and rate flows when one-fourth, one-half, three-fourths, and one whole tablet was used. A whole tablet contains sodium bicarbonate (1.78 gm.), citric acid (0.90 gm.), and tartaric acid (0.90 gm.). The volume of carbon dioxide obtained from effervescence of this tablet is sufficient for uterotubal insufflation in all cases.

After trying different devices for containing the effervescent tablet and the amount of water required for the effervescence, the volume of carbon dioxide thus produced was measured by the siphon volumeter of the Becker-Rubin apparatus and the pressures obtained were simultaneously recorded. A 30 lb. gauge was found to be sufficient for all trials. The highest level of pressure reached when the entire volume of carbon dioxide produced by full effervescence of the tablet was contained within the cup having a capacity of 30 cc. was more than 15 lb., a driving force adequate for the purposes of uterotubal insufflation. In order to reduce the pressure produced by the effervescence to practical

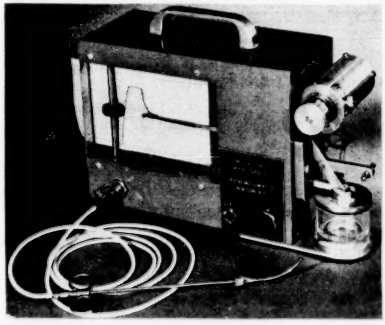

Fig. 3.—Insufflation apparatus, with plastic cup in place closed by toggle clamp and cap, insuring gas-tight circuit for insufflation.

levels, it was found necessary to use a primary pressure limiter, which does not permit the carbon dioxide to exceed a pressure of 300 mm. Hg. From the pressure limiter, a flow control valve controls the rate of flow to the secondary pressure limiter governing the oscillations

4. Bonnet, L.: Usefulness of Measuring Output for Study of Stenosis of Fallopian Tubes by Tubal Kymographic Insufflation, Gynéc. et Obst. **38**: 265, 1938.

5. Sharman, A.: Some Lessons from 4,000 Uterotubal Insufflations, Brit. M. J. **1**: 239, 1954.

6. Marbach, A. H.: Automatic Recording Apparatus for Tubal Insufflation, Am. J. Obst. & Gynec. **39**: 1072, 1940.

7. Weisman, A. I.: A New Multipurpose Apparatus for Use in the Diagnosis and Treatment of Sterility in the Female, Am. J. Obst. & Gynec. **54**: 145, 1947.

in pressure recorded by a writing pen. The total weight of these parts is relatively small. The smaller type of Grafax kymograph, because of its light over-all weight and simplicity in operation, has been admirably adapted to use of the effervescent tablet (fig. 2 and 3). The new apparatus, thus assembled, consists of the following parts (fig. 4): (1) tablet of sodium bicarbonate with citric and tartaric acids, (2) carbon dioxide chamber, (3) closure cap, (4) pressure-limiting bellows, (5) flow-control valve, (6) pressure-recording manometer, (7) kymograph, and (8) outlet to uterine cannula.

The carbon dioxide chamber is a small removable plastic container of 30 cc. capacity made of durable acrylic plastic of suitable size and shape to receive a tablet plus 4 cc. of water. The closure cap serves to seal off the open top of the carbon dioxide chamber after the tablet has been dropped in. It is attached to the instrument by means of a "toggle" clamp (fig. 4*J*) so that the cap can be opened and closed by simply raising and lowering a small lever. Placed immediately above the carbon dioxide chamber, the pressure-limiting bellows (fig. 2 and 3) prevent the pressure delivered to the insufflator from rising above 300 mm. Hg. The flow-control valve is a stainless steel needle constructed to permit controlled flow of carbon dioxide through the valve. Once the stop is adjusted on the dial for the correct rate of flow, it repeats the same rate each time the valve is turned to the "on" position at the point that has been found by trial to deliver the desired rate flow, i. e., that which produces an elevation of pressure not greater than 100 mm. Hg in five seconds.

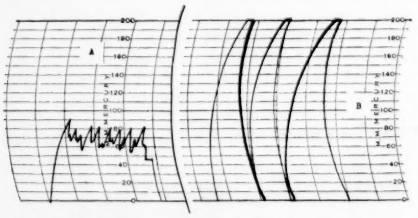

Fig. 5.—*A*, insufflation curve of normal tubal patency and function. *B*, graph typical of tubal nonpatency.

A metallic bellows is used as the actuator for the writing pen mechanism for the pressure-recording manometer. This bellows also has built into it a pressure limiter that does not permit the maximum pressure to exceed 215 mm. Hg. The "V" type recording pen uses ordinary ink and is in contact with the paper because of gravity. No springs or adjustments are needed to make this contact. The chart paper used is of the continuous roll type (60 hours' running time) powered by a silent synchronous motor. As the recording of the test is made, the paper moves out of the instrument and can be cut off by simply pulling against a built-in knife edge (fig. 2 and 3).

A Luer lock connects the outlet tubing of rubber 36 in. long and 3 mm. in caliber with the uterine cannula. A Swinney filter is interposed between the tubing and the cannula in order to exclude bacteria and spores. This filter is inexpensive and is sterilized in the autoclave wrapped in paper or aluminum foil. When a Swinney filter is not available, a test tube containing antiseptic solution may serve to wash the carbon dioxide bubbles. This precaution, although not absolutely necessary, is recommended for safety. It has not been used in older apparatus, and no contamination effects have been observed. Clinical experience with the effervescent tablets lacking the filter has so far been without untoward sequelae.

The oscillations resulting from carbon dioxide insufflated through the uterus and tubes as generated by the effervescent tablet are the same as are obtained when the carbon dioxide flows from a compressed tank. The patient's pelvic sensations, the tubographs (fig. 5), the auscultatory findings, the subjective sense of percolation, and the presence of a subphrenic pneumoperitoneum are also just as characteristic when the tubes are found to be patent as after the test carried out with the older types of insufflation apparatus. The shoulder pains have been observed to be less intense, due possibly to humidification of the effervescent carbon dioxide bubbles, which are probably more rapidly resorbed.

SUMMARY

A new insufflation apparatus has been devised for use in the Rubin test; this has all the essentials of the old competent apparatus, with the advantages of smaller size and weight due to adoption of an effervescent tablet having a known potential quantity of carbon dioxide for each test. The effervescent tablet containing sodium bicarbonate, citric acid, and tartaric acids in suitable proportions as the source of carbon dioxide supply has made possible the elimination of gas tanks, heavy pressure-reducing valves, and reserve chambers. The new kymographic uterotubal insufflation apparatus has been designed to make its use more economical and to make it more generally applicable to the diagnosis and treatment of sterility due to tubal obstruction.

911 Park Ave. (21).

OCCLUSION OF BOTH INNOMINATE VEINS

RESTORATION OF BLOOD FLOW BY ARTERIAL GRAFT

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Lawrence Reynolds, M.D.
and
Forest D. Dodrill, M.D., Detroit

Obstruction to the blood flow in the larger mediastinal veins has always been recognized as a serious complication with a poor prognosis. While it is not an uncommon condition that is too difficult to recognize, suitable treatment is often an insurmountable problem because of the relative inaccessibility of the veins and the variety of causative factors of the condition. Roberts, Dotter, and Steinberg [1] cited neoplasm as the chief of

From the departments of medicine, radiology, and surgery, Harper Hospital.

1. Roberts, D. J., Jr.; Dotter, C. T., and Steinberg, I.: Superior Vena Cava and Innominate Veins: Angiocardiographic Study, Am. J. Roentgenol. **66**: 341, 1951.

these causes, with syphilitic aneurysm and thrombosis following in that order. Ochsner and Dixon,[2] reviewing 120 cases of superior vena caval obstruction, found 36.6% due to phlebitis, 29.1% to external compression (half of these were associated with mediastinal neoplasm), 23.3% to mediastinitis, and 10.8% of unknown or unstated cause. The axillary and subclavian

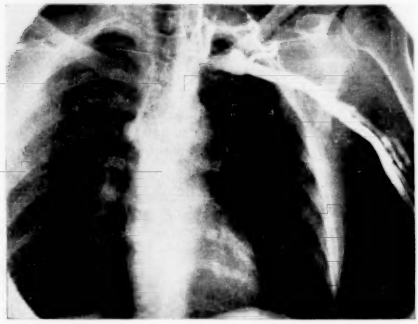

Fig. 1.—Venogram showing obstruction at junction of left subclavian, jugular, and innominate veins.

veins are most frequently involved, according to Veal and Cotsonas[3]; then come the superior vena cava, brachials, innominates, and jugulars. Primary involvement of a single innominate vein is quite rare, and these authors have noted only 11 such cases, all secondary to compression by an aneurysm.

We here report the case of a woman who developed signs of occlusion of the left innominate vein three years after radical mastectomy on the left. Upon mediastinal exploration the right innominate vein was also found occluded. Adequate blood flow was reestablished through an arterial graft connecting the left innominate vein and the superior vena cava.

REPORT OF A CASE

A 48-year-old white woman had fully recovered from a radical mastectomy on the left for scirrhous carcinoma with metastasis to the axillary lymph nodes that had been performed in May, 1951. Three courses of deep x-ray therapy had been given during the following six months. Nearly three years later, in March, 1954, she developed swelling about the right eye with lacrimation, and within the next four weeks her face began to show increasing fulness. At the same time, bending over caused a marked suffusion of the head and neck and she became faint, almost "blacking out" on several occasions while gardening. Gradually there was difficulty with breathing when she was lying flat in bed, so that three pillows were required for comfort. During the next 12 weeks swelling of the left arm appeared and extended downward, involving the forearm and hand. Clusters of purplish venules were now observed over the left chest wall, and the veins of the right breast and along the right anterior axillary line became prominently distended. Finally the left jugular vein also became markedly distended, and the patient was having more dizziness and increasing difficulty with breathing and swallowing. While the face and neck were suffused, there was no cyanosis and the retinal veins did not show distention. Search for metastasis was unrevealing, and x-ray study of the chest showed no significant change in the lungs or mediastinum.

During venography, performed on Aug. 2, 1954, with 70% iodopyracet (Diodrast) injection into one of the veins of the left wrist, the patient developed sudden severe pain just under the middle of the left clavicle so that the injection had to be stopped. Films taken showed obstruction at the junction of the left subclavian, jugular, and innominate veins at the point of greatest pain (fig. 1). This finding, added to the increasing disability of the patient, warranted mediastinal exploration. This was performed on Aug. 5, 1954.

Operation.—With the patient under anesthesia with gas-oxygen-ether, and with curare having been given as a relaxant, operation was performed by one of us (F. D. D.). An incision was made along the course of the left clavicle from the midline of the manubrium. The clavicle was resected subperiosteally and disarticulated at the sternoclavicular junction. The posterior periosteal bed of the clavicle was incised and the proximal two-thirds removed. The hugely distended axillary vein was exposed and dissected down to where it crossed the first rib into the thorax. Since the obstruction was more proximal, the incision was extended down over the sternum to form a hockey-stick and the sternum split down to the third intercostal space. With the spreader inserted, wide exposure of the anterior mediastinum was obtained. Both innominate veins were found obstructed; obstruction on the right was more severe, and the vein was reduced to a fibrous cord about half the size of a lead pencil. The distention of the left innominate vein stopped at about its midportion. Its constriction was due to a perivenous fibrous sheath extending from this point down to the superior vena cava and up around the right innominate vein to above the first rib (fig. 2). Dissection and removal of the fibrous sheath around the left innominate vein was accomplished quite well over its distal aspect, but it was impossible to do this for the right innominate vein, which was totally occluded. On palpating the left innominate vein, a thrombus was found to be present near the junction of the vein with the superior vena cava, extending distally to the junction with the jugular. The vein was incised, and a large mass of thrombus was removed. It was obvious at this point that to establish a venous channel of proper caliber some sort of vascular graft would have to be inserted between the left innominate vein and the superior vena cava. The right innominate vein was freed out to the first rib, tied off, and cut. The constricted portion of the left innominate between the superior vena cava and where its caliber was normal was excised,

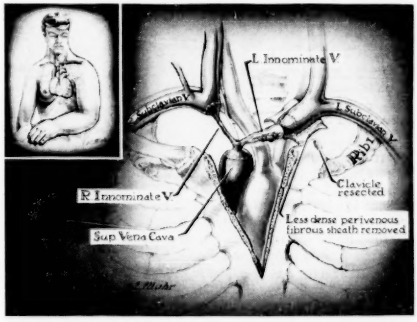

Fig. 2.—Incision and exposure of innominate veins. *Inset*, appearance of patient before surgery.

and a preserved aortic homograft was sutured between these two points (fig. 3). When the clamps were removed, the distention of the left innominate vein had disappeared and there was complete filling and good blood flow through the aortic graft. The pleural openings on the left and right were left for drainage of serum. An intercostal tube was placed in the third right intercostal

2. Ochsner, A., and Dixon, J. L.: Superior Vena Caval Thrombosis: Review of Literature and Report of Cases of Traumatic and Infectious Origin, J. Thoracic Surg. **5**: 641, 1936.

3. Veal, J. R., and Cotsonas, N. J., Jr.: Diseases of the Superior Vena Caval System with Special Consideration of Pathology and Diagnosis, Surgery **31**: 1, 1952.

space for the removal of air and the incision closed airtight. The left half of the manubrium was excised partially so as not to press upon the aortic graft, and the sternal edges were then incompletely approximated for the same reason.

Course.—The patient withstood the six-hour procedure well, and convalescence proceeded without serious setback. On the second day 800 cc. of serosanguineous fluid was aspirated from the left side of the chest, and the tube was removed from the right side of the chest on the third day. The swelling of the left hand started to recede on the second day, and the fulness of the face and distention of the left jugular diminished daily. By the 14th day all swelling had disappeared and the venous clusters on the left chest wall were beginning to fade out. The distended veins over the right breast and axillary region remained unchanged, however. On the 19th day a small area of pitting edema appeared on the lateral edge of the left forearm just below the elbow. This recurred each morning and disappeared at the end of the day. It was believed due to local venous stasis, possibly from the incision in the performance of venography. The arm above this area retained the same size and appearance as was present before the occlusion of the left innominate vein. The patient was discharged on the 31st day. The pathologist's

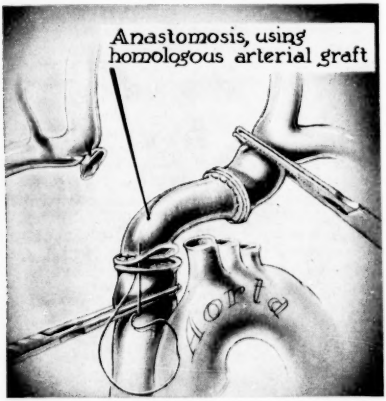

Fig. 3.—Aortic homograft replacing left innominate vein. Right innominate vein has been ligated and cut.

report disclosed that the perivenous fibrous tissue was invaded by undifferentiated carcinoma but that the vein walls had not been so invaded.

Since leaving the hospital the patient has gained in strength and gradually resumed her normal daily activities. Three months after discharge she was totally free of discomfort and the head and neck showed no congestion or venous distention, but edema of the left arm for 3 to 4 in. above and below the elbow recurred at the end of each day. Prominent veins were still present over the right breast and axilla, and purplish clusters of venules were scattered over the left anterior chest wall.

COMMENT

Occlusion of the left innominate vein was suspected in this patient because of the edema of the left upper extremity and the distention of the jugular vein on the same side. That this was due to external compression from metastatic mediastinal lymph nodes was disproved by the negative x-ray findings and the discovery of obstruction to the flow of contrast medium during angiography. However, this failed to account for the uniform swelling of the face, and it was not until the chest was opened that the explanation was found. Evidently the right innominate vein had been slowly occluded by fibrous tissue over a period of time during which collateral circulation was developing. Part of the back flow was being handled by the right lateral thoracic route, as evidenced by the dilated veins in the right chest wall, and probably also by the thyroid veins. The remainder was carried by the left internal jugular and innominate veins. This compromise continued until thrombotic occlusion of the left innominate vein disturbed the balance and precipitated the symptoms described. Increased venous pressure readings would no doubt have been found in both arms, but these were not determined because of inaccessible veins. Angiography was done because it promised more direct evidence as to the nature of the occlusive process.

There were two reasons for the venous occlusion in this case. The primary reason was the perivenous fibrosis that had completely occluded the right innominate vein and was seriously compressing the left. The latter, in turn, was abruptly blocked by a large thrombus. This fibrosis was at first thought due to x-ray therapy after mastectomy, but the finding of invasion by undifferentiated carcinoma that resembled the change found in the primary breast tumor settled the question.

Several methods of treatment have been attempted for occlusion of the large mediastinal veins, particularly the superior vena cava. Shunts to the azygos vein, mediastinal decompression, and venous grafts have met with limited success. Samson [4] reported the case of a 19-year-old boy with superior vena caval obstruction, who, on exploration, was found to have thrombosis of 1 cm. of the superior vena cava and the distal ends of both innominate veins. This area was resected; the left innominate was closed permanently and the superior vena cava closed just above the azygos. An autograft of superficial femoral vein was used with end-to-end anastomosis above and side-to-side anastomosis below; full recovery followed. Scannell and Shaw [5] proposed reconstruction of the superior vena cava by means of a free vein graft for patients in whom superior vena caval obstruction is the result of a benign process. They report a case in which a graft from the superficial femoral vein was used to bridge the gap between the right internal jugular and the right atrium. The graft remained patent, but the patient died of mediastinitis. Kay,[6] in discussing this report, stated that homologous or autogenous transplantation of veins in the treatment of superior vena caval syndrome secondary to chronic fibrosing mediastinitis is not successful. Two of his three patients showed sclerosis of the graft and nonfunction respectively.

Also in this discussion, Hanlon [7] reported the case of a 65-year-old man with malignancy in whom he had performed end-to-end anastomosis of an aortic graft to the right auricular appendage and attached the other end tangentially into the wall of the superior vena cava. The graft remained patent for four months. Deterling [7a] also reported satisfactory results for five months after

4. Samson, P. C., in discussion on Lell, W. A.: Superior Vena Caval Obstructive Syndrome: Report of 3 Cases, Ann. Otol. Rhin. & Laryng. **60**: 754, 1951.

5. Scannell, J. G., and Shaw, R. S.: Surgical Reconstruction of the Superior Vena Cava, J. Thoracic Surg. **28**: 163, 1954.

6. Kay, E. B., in discussion on Scannell and Shaw.[5]

7. Hanlon, R., in discussion on Scannell and Shaw.[5]

7a. Deterling, R. A., in discussion on Scannell and Shaw.[5]

use of an aortic homograft to bridge a 6 cm. defect after excision of an obstructed segment of vena cava. Klassen,[7b] however, found the aortic graft thrombosed one month after its use to replace a constricted vena cava. Gerbode,[7c] outstanding investigator in this field, recounted his experience with 25 animals with homografts: every instance of aortic homograft was followed by thrombosis or gradual fibrosis, and in 6 animals with vein homografts fibrosis or scarring also occurred in time. He favors a vein graft, claiming that venous pressure is not great enough to maintain patency in an aortic graft for a time sufficient to allow the host to replace the graft. Holman and Steinberg [8] used an arterial graft successfully for superior vena caval obstruction, with the patient in good condition 10 months afterwards. The choice of an aortic graft was made in our case because we felt it would provide a more adequate dependable channel for both the venous flow on the left side and the back-flow from the right.

SUMMARY

A patient who had had a left radical mastectomy developed distressing symptoms from venous occlusion in the mediastinum three years later. This was at first attributed to pressure from metastatic lymph nodes, but angiography disclosed obstruction within the left innominate vein. Exploration of the mediastinum disclosed perivenous fibrotic constriction and thrombotic occlusion of the left innominate vein and complete fibrosis of the right. Complete relief of symptoms followed the replacement of the constricted segment of left innominate vein by a preserved aortic graft. At the time of writing, this new channel has functioned adequately for three months.

ADDENDUM

The patient was examined and found to be in good health 14 months after operation.

968 Fisher Bldg. (2) (Dr. Reveno).

7b. Klassen, K. P., in discussion on Scannell and Shaw.[5]
7c. Gerbode, F. L., in discussion on Scannell and Shaw.[5]
8. Holman, C. W., and Steinberg, I.: Treatment of Superior Vena Caval Occlusion by Arterial Graft: Preliminary Report, Clinical Notes, J. A. M. A. **155**: 1403 (Aug. 14) 1954.

SHUNT GRAFT WITH RESECTION FOR ANEURYSM OF ARCH OF AORTA

Herbert D. Adams, M.D., Boston

As our experience with resection and replacement with homologous graft of the abdominal aorta has increased, we have turned our attention to the possibility of the management of aneurysms at higher levels, such as the arch and the descending thoracic aorta. There is one important difference, however, that makes resections of the arch and thoracic aorta hazardous. This is the fact that, with the exception of coarctation, with its massive collateral circulation, it is not possible to shut off the thoracic aorta for a period of time necessary to resect a complicated aneurysm and insert a graft without irrevocable damage to the spinal cord. Aneurysmorrhaphy or plastic sacculectomy, maintaining a functional channel through the aorta during these procedures, has been accomplished in some cases, but in many of these it is fraught with great danger except in the smaller, readily mobilized saccular type. There is the constant danger, during the mobilization and manipulation of the sac, of breaking off the thrombotic material, which may be swept peripherally to block the abdominal aorta and produce irrevocable spinal cord damage. For this reason and others, therefore, it becomes necessary to establish a bypass shunt before proceeding to the actual resection of the large complicated aneurysms, particularly of the arch of the aorta.

A functioning shunt, utilizing a full-length homologous thoracic aorta, can be established by an end-to-side anastomosis with the ascending aorta proximally, employing a large Pott's clamp, and an end-to-side anastomosis with the descending thoracic aorta well below the aneurysm (fig. 1), using a smaller Pott's clamp. If the ascending aortic wall is badly diseased and friable and therefore dangerous to use for such an anastomosis, the left subclavian artery can be safely transected and an end-to-end anastomosis made with the graft proximally and an end-to-side anastomosis below the aneurysm as before (fig. 2). Once good flow is established through this shunt, clamps can then be applied proximal and distal to the aneurysm; the aneurysm can then be resected and the aortic ends closed. The homologous graft shunt remains as a permanent new aortic channel (fig. 3). We have recently applied, with success, these principles to a huge syphilitic aneurysm of the arch, which, in 1952, before we had considered using grafts for this purpose as just outlined, we had treated by combined wire pack and polyethylene wrapping.

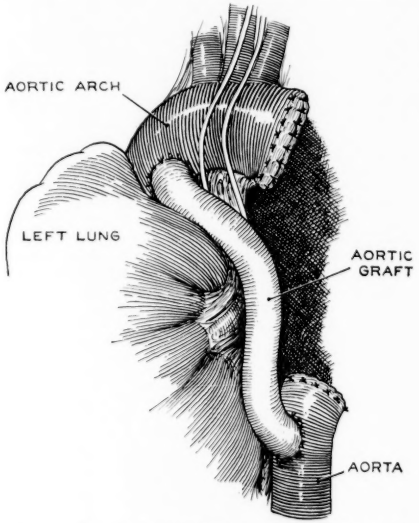

Fig. 1.—Aortic graft established between ascending aorta and aorta distal to aneurysm.

From the Department of Surgery, Lahey Clinic.

REPORT OF A CASE

A 56-year-old woman was first seen on April 30, 1952. She had had syphilis since 1941 and had received treatment until 1950. In October, 1950, she had her first attacks of dyspnea and chest distress, and her roentgenogram was reported as

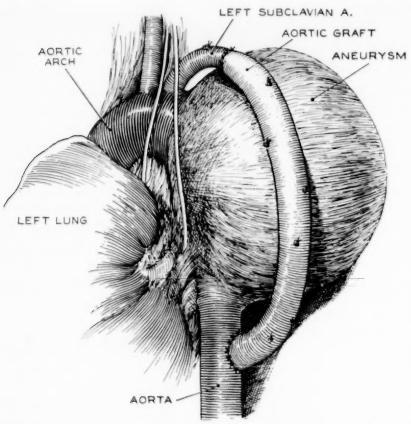

Fig. 2.—Functioning aortic graft established between left subclavian artery and aorta distal to aneurysm prior to resection of aneurysm.

showing an aneurysm at that time. In February, 1951, she was given a course of penicillin treatment, but it was stopped because of a questionable reaction. In October, 1951, she began to have increasing occurrence of choking sensation, dysphagia, nervousness, and increasing chest pain and dyspnea. Roentgenograms

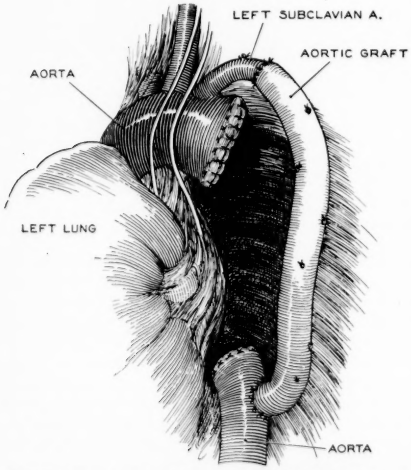

Fig. 3.—Relationship of aortic graft to aorta after resection of aneurysm.

taken at the clinic in April, 1952, showed a huge aneurysm of the arch of the aorta displacing the esophagus and trachea anteriorly, with erosion of the bodies of the fourth to the sixth thoracic vertebrae, inclusive. She was advised to have surgical intervention and was admitted to the hospital on June 14, 1952. On June 16, 1952, the aneurysm was exposed transthoracically, approximately 400 ft. of no. 30 alloy steel wire was packed into the aneurysm, and all of the exposed surfaces were covered with the irritative type of polyethylene. She did well, and her symptoms diminished after this procedure.

In June, 1954, however, the patient returned because of the development of recurrent attacks of pain in the left upper thorax, with considerable nervousness, dyspnea, and general debilitation. Roentgenograms at that time showed increase in the size of the aneurysm; the trachea was displaced to the under surface of the sternum; and the bodies of the fourth to the sixth thoracic vertebrae were almost totally destroyed (fig. 4). She was readmitted to the hospital on July 5, 1954. On July 7, a shunt bypass using an homologous thoracic aorta was established, utilizing the subclavian artery, since attempts to utilize the ascending aorta proved inadvisable owing to the great friability of this structure at this level. With the functioning shunt established in this manner, the aneurysm was totally resected and the ends of the aorta closed, and the shunt continued to function satisfactorily. How-

Fig. 4.—Lateral roentgenogram showing huge aneurysm of arch of aorta with erosion of upper thoracic vertebrae. Wire pack inserted at previous operation can be clearly visualized.

ever, since this patient was an extremely poor risk because of advanced debility, weighing less than 100 lb. (45 kg.) and having greatly reduced cardiopulmonary function of many years' duration, she immediately began to have difficulty in elimination of bronchial secretions. The aneurysm had produced paralysis of the left recurrent nerve and, therefore, since she had such extreme difficulty in eliminating secretions, a tracheotomy was done. In spite of this, bilateral bronchopneumonia developed, and she finally died of pneumonia and pulmonary edema two weeks after operation. At postmortem examination, the cause of death was found to be bronchopneumonia. The graft was intact and had been functioning satisfactorily.

SUMMARY AND CONCLUSIONS

In the surgical management of aneurysms of the arch and thoracic aorta, it is technically possible to establish a shunt bypass utilizing an homologous thoracic aorta anastomosed proximally either to the ascending

aorta or to the left subclavian artery and to resect large, complicated aneurysms in this region. It is our opinion that this is the method of choice in the treatment of aneurysms in the arch of the thoracic aorta, as has proved to be true in the management of aneurysms of the abdominal aorta.

ADDENDUM

Since this paper was submitted for publication, I have successfully employed this technique in an additional case at the United States Naval Hospital, Chelsea, Mass.

A man, aged 30, sustained a severe crushing injury to the chest. He was originally treated for severe shock and extensive hemothorax; he made good recovery and became asymptomatic. About a year later, on routine chest examination, the roentgenogram revealed a large mediastinal mass lying immediately below the arch of the aorta. At operation, a large, thin-walled, saccular, aortic aneurysm just distal to the subclavian artery was exposed. A shunt, utilizing an homologous aorta, was established around the aneurysm, extending from the subclavian artery to the thoracic aorta below the aneurysm. When this shunt was functioning, the aorta was cross clamped proximal to the aneurysm and close to the origin of the subclavian artery and also was cross clamped distal to the aneurysm but proximal to the distal end of the shunt. The aneurysm was resected, and an homologous aortic graft was anastomosed to the resected ends of the aorta. When the clamps were removed and circulation reestablished through the grafted aorta, the shunt was removed. This patient made a satisfactory, complete recovery without vascular or neurological complications.

605 Commonwealth Ave. (15).

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PERIPHERAL NEURITIS FOLLOWING ISONIAZID THERAPY

APPEARANCE OF DUPUYTREN'S CONTRACTURE AND RAYNAUD'S PHENOMENON

Robert A. Hines, M.D., Madison, Wis.

Several articles have appeared describing the neurotoxic effects of isoniazid (isonicotinic acid hydrazide).[1] The disorder is primarily peripheral in distribution, with the stocking-and-glove type of sensory changes. If administration of isoniazid is continued, the symptoms increase in severity and extend to more proximal portions of the extremities. Motor symptoms tend to be mild. Reflex changes when present vary; hyperactivity to complete loss of the deep tendon reflexes have been described. If administration of the medicament is discontinued soon after the appearance of these symptoms, the symptoms have been found to disappear. In the more severe cases, the symptoms tend to persist. The B vitamins, excepting pyridoxine, have been used to counteract these reactions without notable effect. The studies of Biehl and Vilter [2] demonstrated increased urinary excretion of pyridoxine in cases of neuritis caused by isoniazid. The excretion of pyridoxine increased proportionately with the dosage of isoniazid. With high doses of isoniazid (20 mg. per kilogram of body weight), 40% of 20 patients developed peripheral neuritis, while in a similar group receiving a pyridoxine supplement neuritis did not occur.

During the past 18 months, there have been a number of cases of progressive neuritis at the Veterans Administration Hospital, Madison, Wis. The patients were given isoniazid in the usual dosage of 3 to 5 mg. per kilogram of body weight. The occurrence of disabling contractures and Raynaud's phenomenon in three of these cases is the basis of this report.

REPORT OF CASES

CASE 1.—A 61-year-old Negro male was admitted to the hospital on March 31, 1953. Constitutional symptoms of pulmonary tuberculosis had been present since October, 1952. He was not well oriented mentally and developed paranoid ideas while in the hospital. He had far-advanced pulmonary tuberculosis with cavitation. Initially, treatment consisted of streptomycin, 1 gm. twice a week, and aminosalicylic acid, 12 gm. daily. He was unable to tolerate the latter, and, on April 17, 1953, therapy with isoniazid, 100 mg. three times a day, was begun. Within two months, severe pains developed in the hands and feet. The isoniazid was not given for 20 days, and there was a slight improvement. When it was again given neuritic symptoms returned. The dosage was reduced to 50 mg. three times a day, and that dosage continued until the patient was transferred to a hospital for mental diseases on April 22, 1954. While receiving a reduced dosage of isoniazid, the patient continued having neuritic pains. Tender swellings appeared in all fingers, suggesting rheumatoid arthritis. During the next several months, marked flexion contractures developed (fig. 1), in spite of salicylates, splints, and vigorous physical therapy.

Fig. 1.—Severe flexion contractures, resembling Dupuytren's, with tendon thickening in the distal portion of palms of 61-year-old man (case 1) after use of isoniazid in treatment of tuberculosis.

CASE 2.—A 63-year-old white male had far-advanced pulmonary tuberculosis and marked emphysema. His pulmonary tuberculosis was complicated by arteriosclerotic heart disease with auricular fibrillation. He was treated with isoniazid, 100 mg. three times a day, and aminosalicylic acid, 12 gm. daily. Within two months, bilateral muscular weakness in the arms

From the Veterans Administration Hospital.

1. Gammon, G. D.; Burge, F. W., and King, G.: Neural Toxicity in Tuberculous Patient Treated with Isoniazid (Isonicotinic Acid Hydrazide), A. M. A. Arch. Neurol. & Psychiat. **70**: 64 (July) 1953. Lubing, H. N.: Peripheral Neuropathy in Tuberculosis Patients Treated with Isoniazid, Am. Rev. Tuberc. **68**: 458 (Sept.) 1953.

2. Biehl, J. P., and Vilter, R. W.: Effect of Isoniazid on Vitamin B_6 Metabolism: Its Possible Significance in Producing Isoniazid Neuritis, Proc. Soc. Exper. Biol. & Med. **85**: 389 (March) 1954.

was noted, although the patient did not complain of pain. At this time, there was some atrophy of the intrinsic muscles of the hands. Soon stiffness of the fingers was noted, followed by flexion contractures. Sensory examination now revealed areas of hypesthesia in the hands and forearms. The skin of the hands was cool and showed trophic changes and patchy areas of cyanosis.

CASE 3.—A 48-year-old white male was admitted to the hospital on July 21, 1953, with pulmonary tuberculosis. Constitutional symptoms were present for nine months, associated with a 55 lb. (25 kg.) weight loss. Initially he was treated with streptomycin, 1 gm. twice weekly, and aminosalicylic acid, 12 gm. daily. Starting on Aug. 15, 100 mg. of isoniazid was given three times a day because of severe gastroenteritis from aminosalicylic acid. Five weeks later the patient complained of numbness and tingling in the feet and hands. The use of isoniazid was discontinued for 10 days without improvement. Therapy with the drug was resumed, and three months later trophic changes appeared in the skin of the hands, followed by cold

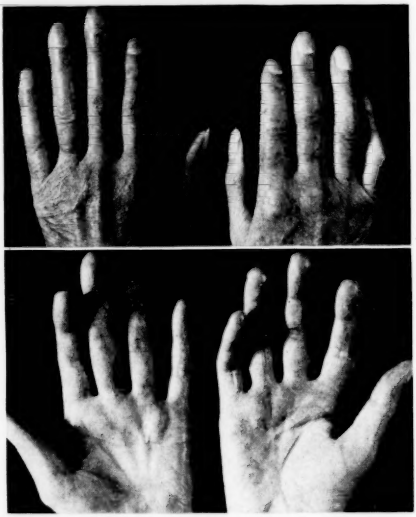

Fig. 2.—Hands of 48-year-old man (case 3) after administration of isoniazid in treatment of tuberculosis. Contracture is most marked in the little fingers. Thickening is present about the common flexor tendon sheath in both palms. A patchy cyanosis is present in the distal portions of the fingers.

sensitivity with cyanosis. In January, 1954, stiffness of the fingers occurred and was followed by thickening along the palmar tendon sheaths and flexion contractures of both little fingers (fig. 2). Use of isoniazid was discontinued on May 27, 1954, and administration of pyridoxine, 100 mg. daily, begun. To the time of writing there has been little change in symptoms or signs.

COMMENT

The common physical findings in these patients were hypesthesia, cyanosis, trophic changes, and contractures. X-rays of the hands of the patient in case 2 were suggestive of early changes of rheumatoid arthritis, while those in the patient in case 3 revealed only slight generalized osteoporosis. No other evidence was found to substantiate a diagnosis of rheumatoid arthritis in this case. The absence of sensory complaints of the patient in case 2 was unusual, but the end-results were rather typical of a peripheral neuritis. The presence of Dupuytren-like contractures in these cases is associated with severe neurotrophic and Raynaud's phenomenon. The Raynaud's phenomenon with coldness and cyanosis was considered secondary to vasospasm. This has been described as occurring in peripheral neuritis.[3] It is presumably due to inhibition of axon reflexes from peripheral nerves supplying vasodilator impulses.

The occurrence of Dupuytren's contractures in neurovascular disturbances is well known. Under the heading of "reflex dystrophy of the upper extremity," a variety of contractures has been described.[4] In this condition one encounters a pathological process arising in various locations, setting up a reflex discharge of sympathetic impulses to the upper extremity. This leads to the development of vascular disturbances and contractures. The other explanation would be a direct stimulation of the autonomic nervous system as postulated by Selikoff, Robitzek, and Ornstein.[5] They based their conclusions on the findings of dizziness, insomnia, constipation, and urinary retention occurring in several patients who were receiving 1-isonicotinyl-2 isopropyl hydrazine (Marsilid). Fisher and others [6] also demonstrated evidence of temporary vasospasm occurring in 5 of 23 patients receiving isoniazid and 1-isonicotinyl-2 isopropyl hydrazine.

SUMMARY

Three patients being treated for tuberculosis developed Dupuytren-like contractures and Raynaud's phenomenon following isoniazid neuritis. It is believed that these changes are caused by disturbances of a neurovascular nature developing secondary to the use of isoniazid.

2500 Overlook Terrace.

3. Edwards, E. A.: Varieties of Digital Ischemia and Their Management, New England J. Med. **250**: 709 (April 29) 1954.

4. Steinbrocker, O.; Spitzer, N., and Friedman, H. H.: Shoulder-Hand Syndrome in Reflex Dystrophy of Upper Extremity, Ann. Int. Med. **29**: 22 (July) 1948.

5. Selikoff, I. J.; Robitzek, E. H., and Ornstein, G. G.: Toxicity of Hydrazine Derivatives of Isonicotinic Acid in Chemotherapy of Human Tuberculosis: Preliminary Report, Quart. Bull. Sea View Hosp. **13**: 17 (Jan.) 1952.

6. Fisher, M. M., and others: Isonicotinic Acid Hydrazide and Its Derivatives in Tuberculosis: An Evaluation of the Side-Effects in Relation to Peripheral Circulation: Preliminary Report, New York J. Med. **52**: 12 (June) 1952.

ASPIRATION BIOPSY OF THE KIDNEY

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and
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There are many instances in diagnostic medicine and also in clinical research when correlation of renal function and a clinical syndrome with the exact renal histopathology would be valuable indeed. Needle biopsy of the liver, the spleen, the prostate, and the lung have been performed because of a similar need in other fields. Needle biopsy of the kidney was first performed by Iversen and Brun in 1951.[1] Since then, several reports [2] of its use have appeared in the literature. It is the purpose

From the Department of Surgery, University of Oregon Medical School.

1. Iversen, P., and Brun, C.: Aspiration Biopsy of the Kidney, Am. J. Med. **11**: 324-330, 1951.

of this paper to report our experiences with this technique.

MATERIALS AND METHODS

Materials used were: the Turkel liver biopsy needle, consisting of an outer needle and stylet, 11 gauge, 100 mm. long, with an adjustable guard control, and an inner trephine needle and stylet, 13 gauge, 150 mm. in length;

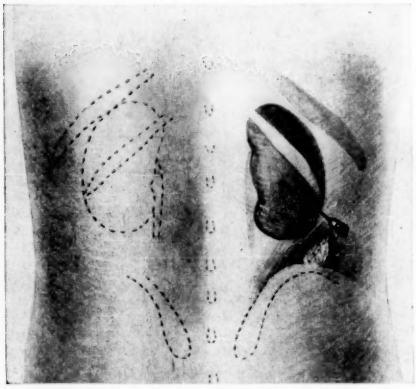

Fig. 1.—Topographic anatomic relations of kidneys.

20 cc. syringe for the aspiration biopsy; 10 cc. syringe for procaine infiltration; one no. 18 needle, a no. 25, and a long no. 22 needle; no. 15 Bard-Parker scalpel blade and handle; one curved Kelly hemostat; large sterile drape with a central aperture; and prep sponges. In addition, one needs 1% procaine, a skin disinfectant, and a wide-mouthed specimen jar with formaldehyde for immediate fixation of the specimen. A long no. 16 needle with a serrated tip and obturator is included for kidney biopsy in children.

An intravenous or retrograde pyelogram is obtained, if possible, for accurate localization of the kidneys and to rule out malposition or absence of the kidney. On the pyelogram we measure the relationship of the inferior pole of the kidney to the vertebrae and to the 12th rib (fig. 1 and 2). The right kidney is preferred because of its lower position and the presence of the spleen on the left; biopsy of the left kidney has been done, however, without incident. In the average individual, six finger-breadths are measured from the midline and two finger-breadths inferior to the 12th rib at that point. This avoids the intercostal arteries. The biopsy is usually done at the bedside, with the patient sitting erect and the legs over the edge of the bed. The selected site is prepared with an antiseptic solution, a procaine skin wheal raised, and a sterile drape placed about the field. After deep infiltration of the area, a small skin incision is made. The trocar is next introduced. Our initial misses resulted from angling the needle too much medially or too far cephalad. A satisfactory rule of thumb to follow is to direct the needle perpendicular to the curve of the flank and in the horizontal plane. As the trocar advances through the fascial layers, a definite snap is usually felt as the lumbodorsal fascia is penetrated. Almost immediately the needle will encounter a solid mass, presumably kidney. After several biopsies have been performed, this is more readily recognized. To the exploring needle this has the consistency of a soft rubber ball and moves against the needle with inspiration. The needle is impinged into the kidney substance for a few millimeters only. If the needle is in the kidney, the hub will traverse a distance of 2.5 to 5.1 cm. with each respiratory cycle. If this does not occur, the needle is probably not in the kidney and a reinsertion is indicated. The obturator is now removed, and the inner needle with the serrated tip is inserted until the kidney is felt. The 20 cc. syringe is next attached and negative pressure applied. While maintaining suction on the syringe with the right hand, the needle is advanced and rotated simultaneously for a distance of 3 to 5 cm. (fig. 3). While still maintaining negative pressure in the syringe, the needle and cannula are removed together. As soon as the needle tip reaches the skin, a sliver of renal tissue will be aspirated into the syringe. This varies in size from a small fragment to enough tissue for a good biopsy measuring 4 cm. and including renal capsule and an entire section of cortex and medulla with a small fragment of pelvis epithelium (fig. 4). The needle is detached and the specimen expelled into the formaldehyde specimen jar.

RESULTS

Our results varied with the number of procedures performed. Initially our success was only 30%, but later it ranged up to 80% in the last series of 10 biopsies. A total of 44 biopsies was performed, with a successful biopsy being obtained in 24, an over-all percentage of

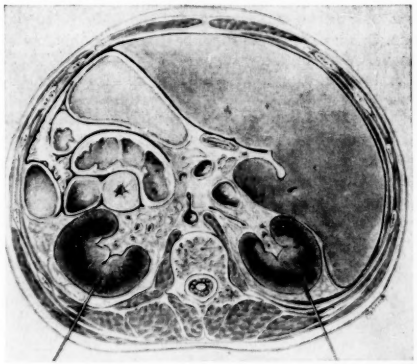

Fig. 2.—Cross sectional anatomic relations of kidneys with kidney biopsy needle in place.

success of 54.5%. Success was determined by obtaining a large enough specimen so that a satisfactory histological study could be made. Our percentage of success

2. (*a*) Parrish, A. E., and Howe, J. S.: Needle Biopsy as an Aid in Diagnosis of Renal Disease, J. Lab. & Clin. Med. **42**: 152-157, 1953. (*b*) Kark, R. M., and Muehrcke, R. C.: Biopsy of Kidney in Prone Position, Lancet **1**: 1047-1049, 1954. (*c*) Bjørneboe, M., and others: Nephrotic Syndrome: Histological Changes Illustrated by Means of Biopsy of the Kidney, Acta med. scandinav. (supp. 266) **142**: 233-248, 1952. (*d*) Greenwald, H. P., Bronfin, G. J., and Auerbach, O.: Needle Biopsy of the Kidney: Report of 5 Cases of Multiple Myeloma, Am. J. Med. **15**: 198-206, 1953.

compares favorably with that of Iversen and Brun,[1] who reported success in 42 of 80 biopsies, and with Parrish and Howe,[2a] who reported 29 successful biopsies in 50 attempts. Kark and Muehrcke,[2b] however, recently reported 48 successful biopsies in 50 attempts using the Vim-Silverman needle with the patient in the prone posi-

Fig. 3.—Biopsy needle is advanced and rotated with negative pressure maintained within syringe.

tion. Our unsatisfactory biopsies included the finding of only fatty tissue, fibrous tissue, liver (in three), insufficient renal tissue for diagnosis, or no tissue being obtained.

COMPLICATIONS

A transient hematuria seemed to be a common finding, lasting up to 24 hours. No serious bleeding was encountered; however, a perirenal hematoma necessitating surgical intervention is described by Parrish and Howe. The discomfort to the patient is usually limited to a short, sharp pain, deep within the loin, at the time of biopsy. Some patients have noted persistent mild discomfort for up to 12 hours. One patient described severe flank pain radiating into the right testis. Nausea and vomiting have also been noted but are unusual. Other theoretical complications, so far not encountered, would seem to include perforation of an intra-abdominal viscus, dissemination of a tuberculous or malignant process, infection, rupture of a renal cyst, or stimulation of a neurovascular renal reflex. Contraindications arrived at from these real and theoretical complications include a bleeding tendency, suspected malignancy or tuberculosis, or a suspected perinephric abscess. Excess obesity or an uncooperative patient also contributes to failure.

REPORT OF CASES

The following cases are three examples in which renal aspiration biopsy was used as an additional aid during urologic study.

Case 1.—A 76-year-old male was admitted to the hospital with a two year history of chronic prostatism culminating in acute urinary retention. Physical examination revealed hypertension with blood pressure of 194/90 mm. Hg, arteriosclerotic heart disease, chronic bronchitis, and benign prostatic hypertrophy. Urinalysis revealed 1+ albuminuria, 3+ hematuria, 2+ pyuria, and granular casts. The blood urea nitrogen was 27 mg. per 100 cc. To evaluate the degree of this patient's chronic renal damage, renal biopsy was performed. The specimen consisted of a piece of tissue 1.5 cm. in length and uniformly 2 to 3 mm. in diameter. Histologically there were noted large areas of scarring, tubular and glomerular atrophy, and scattered areas of chronic inflammation. The diagnosis was chronic pyelonephritis. The patient had an uneventful transurethral prostatectomy.

Case 2.—An 81-year-old male with diabetes was admitted to the hospital with acute urinary retention. Physical examination revealed moderate hypertensive cardiovascular disease, blood pressure of 180/80 mm. Hg, and benign prostatic hypertrophy. The urinalysis revealed 1+ albuminuria, 4+ pyuria, and bacilluria. The blood urea nitrogen was 19 mg. per 100 cc. Because of the patient's diabetic history and chronic urinary tract obstruction, it was thought that evaluation of the patient's renal histology would be prognostically helpful. The specimen consisted of a tubular segment 2.5 cm. in length. Histologically, multiple foci of scarring were seen in the cortex, many atrophic and other dilated tubules were identified, and varying degrees of chronic inflammation were found. Diagnosis was chronic pyelonephritis. The patient had an uneventful transurethral prostatectomy.

Case 3.—A 71-year-old male was admitted with symptoms of long-standing prostatism and a residual urine of 475 cc. Physical examination showed moderate arteriosclerotic heart disease, blood pressure of 180/92 mm. Hg, emphysema, and benign prostatic hypertrophy. Urinalysis revealed 2+ albuminuria, 4+ pyuria, and numerous bacteria. The blood urea nitrogen was 32 mg. per 100 cc. Preoperatively urethral catheter drainage was instituted; however, the uremia was progressive to a maximum blood urea nitrogen of 63 mg. per 100 cc. Renal biopsy revealed numerous foci of chronic inflammation, hyalinization of vessels, and marked scarring with atrophy and dilatation of the tubules. Diagnosis was chronic pyelonephritis. Because of the severe degree of renal damage, nonsurgical management was elected, and the patient was discharged but catheter drainage was continued at home.

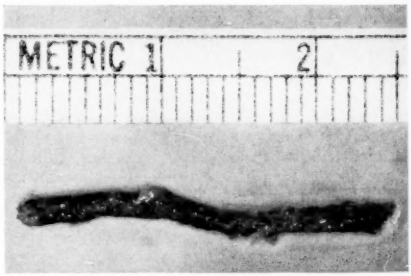

Fig. 4.—Approximate size of good aspiration biopsy.

COMMENT

Although our series and experience with renal aspiration biopsy are much too meager to draw any statistically significant conclusions, certain impressions were obtained. The value of obtaining exact histopathological information in chronic renal disease or in studying the milder or the acute forms of renal disease seemed self-evident. However, after having the procedure available,

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many previously accepted renal situations appeared in which biopsy was an appealing adjunct. The list includes evaluation of renal disease in the hypertensive patient, exact diagnosis in the patient with nephrosis, the degree of nephropathy associated with the patient in the diabetic state, renal disease in the patient with eclampsia, and, as in our cases, the marked but infrequently emphasized degree of chronic pyelonephritis in chronic urinary tract obstruction. Immediate and accurate diagnosis in acute renal insufficiency seemed to be a particularly fertile field for both prognosis and clinical research.

The procedure is simple, technically, although accuracy is not yet predictable, and requires only the usually available biopsy instruments. We prefer to use the Turkel needle and an aspiration type of biopsy, but acceptable modifications of the Vim-Silverman needle are now also available. A sufficient degree of skill can soon be acquired by anyone who will briefly review the anatomy of the region. It is safe for the patient; the

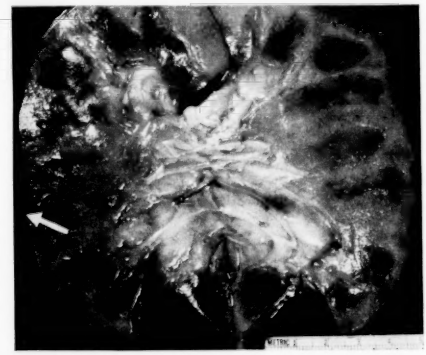

Fig. 5.—Needle tract (arrow) in bisected kidney of patient on whom aspiration biopsy was performed and who died from unrelated causes.

number of complications reported in over 250 biopsy attempts now in the literature is negligible. Perirenal or retroperitoneal hemorrhage was anticipated but has not occurred. Autopsies on patients who had had renal biopsy and who had died for unrelated causes were performed in three instances. Bleeding at the puncture site in all cases was minimal and, in one, difficult to detect. The potential hazards must be borne in mind, however, and the procedure not used indiscriminately. The greatest drawback at the present time with the technique described has been the unpredictability of success. Familiarity with the procedure progressively improved our results, and with the most recent biopsies success is now anticipated in 80% of the cases attempted. When tissue is obtained, the specimen is remarkably adequate and our pathologists have not complained about insufficient tissue for diagnosis. Damage to the kidney by the biopsy is also minimal and, in those instances where we have been fortunate enough to see the kidney subsequently, the biopsy tract is recognized only as a small, dark red streak (fig. 5).

CONCLUSION

Renal aspiration biopsy is a valuable practical adjunct in the treatment and study of renal disease. It should assume its place with biopsy of other organ systems of the body and be used with caution but not fear when indicated.

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A COLOSTOMY IRRIGATOR OF IMPROVED DESIGN

Eugene H. Weissenberg, M.D.
and
H. M. Thompson, Jefferson Barracks, Mo.

While it is desirable that a colostomy be irrigated daily, the unpleasant nature of the procedure, with the devices at present available, causes many patients to postpone it whenever possible. Employing the ordinary irrigator, a mixture of feces and water may be expelled so forcibly that its confinement to a receptacle is exceedingly difficult. Even if the operation is performed in a bathtub, a distasteful clean-up must necessarily follow. To make this necessary operation less unpleasant, we have modified an applicator used mainly in Europe for colonic irrigation in a bathtub so that a patient himself can manipulate it with no chance of soiling and with a minimum of clean-up afterwards.

Our new device is made of clear plastic and consists of two major parts that join together. A plastic ring is held firmly against the abdomen by a belt attached to two ear-like projections. An interlocking funnel device, also of plastic, fits this ring. The funnel is continuing with a 1 in. (2.5 cm.) outlet tube set at a right angle. A hole 1½ in. in diameter in the side of the funnel is fitted with a rubber stopper through which passes a smaller tube. To the inside of this tube is attached a rubber catheter (16 or 18 F.), while the outside of the same tube bears a rubber hose connected to a hot water bottle and provided with a shut-off clamp (fig. 1).

PROCEDURE OF IRRIGATION

The patient fills the hot water bag and then connects it to the proper rubber tube, which is clamped off. He puts the filled hot water bag on a little stool next to the toilet. While standing, he fastens the plastic ring firmly to his abdomen by pulling the belt tight. Then he sits down to check whether the belt is too tight for the sitting position. If so, he loosens the belt slightly and stands up again. The funnel component is next locked into the ring with a slight turn. Still standing, he inserts the catheter through the hole in the funnel and into the colostomy, pushing it until he can close the hole in the side of the funnel with the stopper to which the catheter

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the results of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

The new all-plastic irrigator can be obtained on order from Technical Enterprises, P. O. Box 456, St. Louis 12.

tubing is fastened. The patient now sits down on the toilet seat so that the plastic angular tube is between his thighs pointing into the bowl. While seated, he connects the hot water bottle to the outside end of the small tube and puts the water bottle upon one thigh. The clamp is opened and the rubber bag pressed against the thigh with one hand, causing the water to enter the colostomy (fig. 2). The patient lifts the hand off the bag

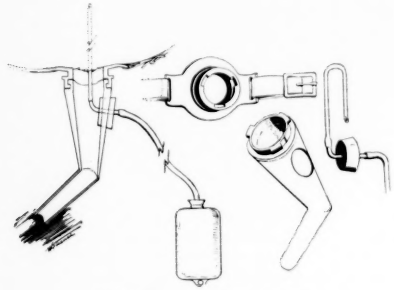

Fig. 1.—Parts of colostomy irrigator.

and closes the clamp when he does not want more water to enter his colon. Later, when water and colon contents are expelled, they are carried through the funnel and the large right angle tube directly into the toilet bowl. The patient may let more water run into his colon by opening the clamp and again exerting pressure upon the rubber reservoir. Closing the clamp, the patient then rests upon the toilet seat until he feels that no more watery feces will be expelled. This may require 20 minutes to an hour and a half. Finally, the patient disconnects the water bag and unlocks the funnel component. With the rubber stopper still wedged in the hole, the catheter is withdrawn from the colostomy as the funnel is removed from the plastic ring and put into a basin. Then the belt is loosened and the ring, too, is put into the basin. All parts are then washed in running water and may be dried and put away or stored under an antiseptic solution.

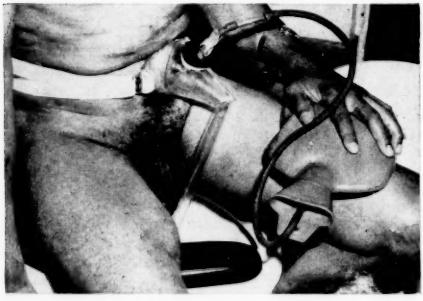

Fig. 2.—Patient using the improved colostomy irrigator.

This improved colostomy irrigator enables a patient to care for his toilet activities with a minimum of effort and inconvenience. It can also be used by the nursing staff while the patient still occupies a hospital bed, the principal difference being that the large drain tube must empty into a bedpan.

FULL-THICKNESS SKIN GRAFT IN THE CLOSURE OF A DEFECT OF THE THORACIC WALL

W. David Dunavant, M.D., Memphis, Tenn.

A free graft of full-thickness skin will live when sutured into a defect in the chest wall and the lung reexpanded. As far as we can ascertain from the literature this is the first time a full-thickness skin graft has been used to close a defect in the chest wall without placing the graft directly on the lung. Defects in the chest wall may result from radical resection of tumors or from trauma. Carcinoma of the breast or lung invading the chest wall or recurrent disease may require resection of a portion of the chest wall. If the defect extends into the pleural cavity the problem of an open pneumothorax exists and a flap of tissue must be made available to form an airtight closure.

Various methods have been devised in the past to repair defects in the chest wall. The opposite breast, muscle, and fascia were used by Maier [1] and Pickrell.[2] Free grafts of fascia lata were employed by Watson [3] and Mayer.[4] The pericardium was sutured into a defect in the chest wall and covered by split-thickness skin graft by Pickrell.[5] Tantalum plates have been used by Effler and Blades [6] and found to be unsatisfactory because they moved, became loose, and sloughed out or had to be removed. Morrow [7] has used tantalum plates successfully in dogs. Tantalum mesh has also been used but may undergo fragmentation due to constant movement of the thoracic cage. Although a full-thickness skin graft would offer little stability, it does offer the surgeon a means by which an airtight closure can be obtained in those defects where no other tissue is readily available. The following case report presents such a patient in whom the other breast or skin flaps could not be used for closure because of such a wide excision of skin and a portion of the chest wall.

REPORT OF A CASE

A 59-year-old Negro woman was seen in the outpatient department of the John Gaston Hospital on April 30, 1951, with the complaint of an ulcerating lesion on the right breast with

From the Department of Surgery, University of Tennessee School of Medicine and John Gaston Hospital.

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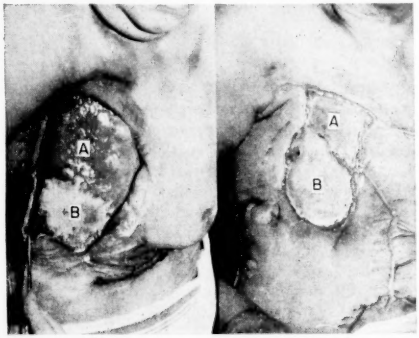
7. Morrow, A. G.: The Use of Tantalum Gauze in the Closure of Full-Thickness Defects in the Chest Wall: Experimental Study in Dogs, Surgery **28**: 1016-1021, 1950.

constant pain. The patient was well until two years before, when she fell and struck her right breast. Following this a small lump was noticed in the lower portion of the breast that soon became asymptomatic. Four months ago the mass began to enlarge and became painful, especially when clothes would rub the lesion. She applied several types of skin paints and salves to the lesion, including iodine and carbolic acid. One month before admission the lesion became ulcerated. On April 28, 1951, she saw her physician for the first time, who referred her to the outpatient department of the John Gaston Hospital where a biopsy of the lesion was performed and revealed adenocarcinoma. On admission examination revealed an elderly, obese woman who did not appear acutely ill. On examination the head and neck were normal. She had hypertension (blood pressure 190/100 mm. Hg) with no evidence of decompensation or other cardiovascular disease. Heart and lungs were normal. There was a firm, hard mass measuring 8 cm. (about 3 in.) in diameter located at the inferior margin of the right breast at the junction of the chest wall. There was an ulceration at the lower border of the mass measuring 1.5 cm. (0.6 in.) in diameter. The mass and area of induration around the mass were firmly attached to the underlying chest wall. There were no supraclavicular nodes palpable, but one node 1 cm. (0.4 in.) in diameter could be felt in the axilla. The rest of the examination was negative.



Left, photograph of the wound on the 14th postoperative day showing *A*, granulating wound on the chest wall to be covered with a split-thickness graft and *B*, full-thickness skin graft covering the defect in the chest wall. *Right*, photograph of the wound on the 30th postoperative day showing *A*, split-thickness skin graft on the chest wall and *B*, full-thickness skin graft covering the defect in the chest wall and covering the lung.

Laboratory studies revealed a red blood cell count of 4,200,000 per cubic millimeter, hematocrit of 24%, and hemoglobin level of 9 gm. per 100 cc. The white blood cell count was 12,450 per cubic millimeter with a normal differential. The urinalysis revealed numerous white blood cells and gram-negative rods. The patient was placed on a high-protein, high-calorie diet supplemented with vitamins. She was given several transfusions and placed on penicillin and streptomycin therapy, with wet dressings applied to the ulcerated lesion. The ulcerated area became clean, regressed in size, and appeared to be healing.

She was operated upon on May 25, 1951, and a radical mastectomy with excision of a portion of the chest wall was performed. After dissection of the axilla, the pectoral muscles were dissected from the chest wall back to the site of the tumor. It was felt that the tumor was adhered to the intercostal muscles and ribs with possible invasion of the chest wall. A section of the chest wall was resected including the fifth and sixth ribs with the underlying pleura from the sternum laterally for a distance of 6 in., 2 in. beyond the gross extent of the tumor. The pleural cavity and lungs were then inspected and found to be free of gross metastasis or nodes. There was no gross evidence of disease along the internal mammary vessels. A full-thickness graft of skin was then obtained from the lateral flap at the upper end of the incision. All subcutaneous tissue was removed from the graft. With the lung collapsed the graft was sutured around the defect, making the pleural cavity airtight. A catheter was placed in the pleural cavity and was brought out through a stab wound lateral to the operative site. The entire wound was then closed as much as possible by swinging the other breast over and closing the skin flaps under tension. There was an area about 3 in. left open, part of the graft being visible. After the wound was closed the catheter was aspirated and the lung reexpanded. The catheter was then removed. A massive pressure dressing was then applied, and the patient was sent to the room in good condition.

Microscopic examination revealed adenocarcinoma with two positive nodes and extension into the deep pectoral fascia but no involvement of the ribs or intercostal muscles. The patient did well postoperatively with no respiratory difficulty, and the chest remained clear on x-ray. On the seventh postoperative day there was necrosis of the skin edges and sloughing and separation of the wound; however, at this time the graft was completely visualized and appeared to be viable. By the 14th postoperative day the open granulating wound was clean and the skin graft viable and intact (see figure, *left*). The chest wall was stable; however, the graft moved with respiration, the lung apparently having become adhered to the graft producing a source of blood supply and a viable graft. On the 24th postoperative day a split-thickness skin graft was placed on the granulating wound of the chest wall and all wounds were healed one month after surgery (see figure, *right*). This patient did well until May, 1953, when she was seen with metastasis of the lung and spine. She died in June, 1953.

COMMENT

A defect in the chest wall was closed with a full-thickness skin graft, and no instability of the chest resulted. The relatively thin covering of the lungs by the graft produced little protection; however, the patient wore a padded prosthesis with no difficulty as long as she lived. We do not know how large a defect could be covered with such a graft and the chest wall remain stable. However, it was no problem in this patient and from observation of this patient one would think that a defect twice this size could be covered with a skin graft without jeopardizing the stability of the chest.

899 Madison Ave.

Adrenal Steroid Therapy.—Although a vast number of clinical observations on the effects of . . . hormonal agents have been made, there is as yet little or no insight into the mechanisms by which these effects are produced and their site of action. It is postulated that there must be some fundamental action on cellular metabolism, which may lead to an alteration in the mechanism of response of the cells to the many unknown factors which lead to disease. Browne's philosophic concept of the "iceberg" theory of disease is a useful one: that, like the iceberg, many organism's responses to disease are similar and submerged below the surface; that the symptoms and signs which we recognize as disease entities are the visible peaks of the iceberg; and that the adrenal cortical hormones tend to alter or "melt away" the submerged portion, causing the visible peak, which is recognized as a disease, to disappear below the surface. As our observations increase we are repeatedly struck by the evidence of progression of the disease in spite of clinical remission. This is particularly true in the mesenchymal diseases, such as rheumatoid arthritis, rheumatic fever and lupus. This progression suggests that one "deviates" the disease but does not alter its basic course. One of the most significant contributions of these agents has been in demonstrating the potential reversibility of complex disease, which should stimulate further inquiry into their pathogenesis with the hope of an ultimate understanding.—J. C. Beck, M.D., The Present Status of ACTH and Adrenal Steroid Therapy in Medicine, *Annals of Internal Medicine*, October, 1955.

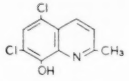
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs that appear in this column have been authorized by the Council for publication and inclusion in New and Nonofficial Remedies. They are based upon the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary*

Chlorquinaldol. — $C_{10}H_7Cl_2NO$. — M.W. 228.09. — 5,7-dichloro-8-hydroxyquinaldine.—The structural formula of chlorquinaldol may be represented as follows:



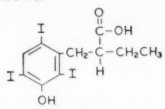
Actions and Uses.—Chlorquinaldol, an oxyquinoline derivative, exhibits the keratoplastic, antibacterial, and antifungal properties shared by other externally applied compounds of this type. Like similar derivatives, its mild antiseptic action may be useful in the topical treatment of minor cutaneous bacterial and mycotic infections. Chlorquinaldol may be more effective against bacterial infections than other isoquinolines, especially for resistant staphylococcic infections of the skin. It also appears to be at least as active against superficial fungal infections as other isoquinolines. The predominating keratoplastic effect of this type of compound may be more significant than its fungistatic action in the management of dermatomycoses.

Chlorquinaldol may produce skin sensitization that follows repeated topical use of other oxyquinoline derivatives. So far it appears to have a lower index of sensitization than other oxyquinoline derivatives such as iodochlorhydroxyquin. Chlorquinaldol may be better suited for local treatment of minor skin infections than certain antibiotics, which are known to produce frequent sensitivity reactions that interfere with their systemic use in serious generalized infections. If skin sensitization appears after repeated application of chlorquinaldol, the agent should be discontinued until such reaction subsides and then, if further treatment is indicated, replaced by some other type of treatment.

Dosage.—Chlorquinaldol is applied topically as a 3 to 5% concentration in a suitable dermatological vehicle. After appropriate cleansing, a cream or ointment may be applied twice daily to affected areas.

Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of chlorquinaldol.

Iophenoxic Acid.—$C_{11}H_{11}I_3O_3$. — M.W. 571.96. — α-Ethyl-3-hydroxy-2,4,6-triiodohydrocinnamic acid.—α-Ethyl-β-(3-hydroxy-2,4,6-triiodophenyl)propionic acid. —The structural formula of iophenoxic acid may be represented as follows:



Actions and Uses.—Iophenoxic acid is a water-insoluble organic iodine compound for oral administration as a radiopaque agent in cholecystography. It produces a reasonably consistent and dense gallbladder shadow for roentgenographic visualization of nonopaque stones and for observing the functional capacity of the gallbladder to concentrate and then expel bile following a high fat meal. It also permits visualization of the extrahepatic ducts after cholecystography. After oral administration, it is rapidly absorbed, eliminated in the bile, and subsequently excreted, chiefly in the urine. Thus it seldom produces opacities in the gastrointestinal tract. An optimal concentration in the gallbladder usually appears within 8 to 12 hours after ingestion of a single dose; the density of the shadow produced with the recommended dose ordinarily does not obscure stones that may be present.

Iophenoxic acid has a low systemic toxicity and a low level of unpleasant side-reactions. Nausea, vomiting, and diarrhea are minimal, rarely severe. Complaints of a burning sensation while swallowing have not been reported, and subsequent dysuria occurs infrequently. As with other systemically administered iodinated compounds, it should be used with extreme caution, if at all, in patients with advanced renal impairment. The calculated risk involved with its use in other conditions in which iodine may be contraindicated, especially when there is known iodine sensitivity, should be weighed against the need for cholecystographic diagnosis.

Dosage.—Iophenoxic acid is administered orally. The usual dose is calculated on the basis of approximately 50 mg. per kilogram (2.2 lb.) of body weight. A dose of 3 gm. is usually adequate for a patient weighing 68 kg. (150 lb.); a dose of 6 gm. should not be exceeded. For cholecystography, the patient is instructed whenever feasible to eat a high fat lunch the day the agent is to be administered to encourage evacuation of the gallbladder so that it may refill with opacified bile; the evening meal should be fat free. The calculated dose is taken with a glass of water at such time during the evening as will permit a 10 hour interval to elapse prior to the time scheduled for roentgenography on the following morning. A fatty meal ingested after the cholecystographic examination usually permits roentgenographic visualization of the extrahepatic ducts 20 to 30 minutes after the meal. If the gallbladder is not visualized following the initial dose and this cannot be attributed to extracholecystic factors, the examination should be repeated the following day with the same dose. Nonvisualization after a second dose usually indicates a pathological condition of the gallbladder.

Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of iophenoxic acid.

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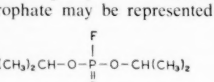
Isoflurophate, U. S. P.—$C_6H_{14}FO_3P$.—M.W. 184.15. — Diisopropyl fluorophosphate. — The structural formula of isoflurophate may be represented as follows:



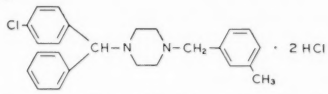
Actions and Uses.—Isoflurophate, a parasympathomimetic agent, acts chiefly by irreversible inhibition of the enzyme, cholinesterase. The anticholinesterase activity of isoflurophate is more prolonged than that of physostigmine and similar drugs; thus it is more convenient for maintaining miosis in the treatment of glaucoma, with fewer instillations. Systemic administration of the drug is contraindicated because this produces a profound reduction of plasma cholinesterase that is associated with prolonged and sometimes serious effects of generalized parasympathetic stimulation, including salivation, lacrimation, intestinal cramps, urge to urinate and defecate, shock, and collapse. In addition to its widespread cholinergic effect, large systemic doses of the drug also produce paralysis of autonomic ganglions that resembles the systemic action of nicotine. When the drug is instilled locally in the eye, plasma cholinesterase is reduced only slightly and seldom is accompanied by systemic effects. Isoflurophate produces a powerful and relatively prolonged miotic action and spasm of the muscles of accommodation caused by the local antagonism of cholinesterase. It is used by corneal instillation to reduce intraocular tension in the treatment of aphakic glaucoma and chronic noncongestive (wide angle) glaucoma, for preoperative control of glaucoma, and as an antidote against the harmful action of atropine on preglaucomatous and glaucomatous eyes. Many ophthalmologists consider the drug to be contraindicated in acute congestive (narrow angle) glaucoma because of the danger of increasing intraocular pressure.

Isoflurophate has a tendency to produce ciliary spasm and, rarely, a rise rather than a reduction in intraocular tension. This latter response probably can be forestalled if tonometric examinations are made hourly after the initial use of the drug, since instillations of 1 or 2% epinephrine solution at 5 minute intervals, following detection of increased pressure, may be successful in preventing any further rise. The ciliary spasm that is produced at times by isoflurophate may cause brow pain and headache that may be minimized and at times eliminated by the use of smaller amounts of the drug. Local sensitivity to the drug or the solvent in which it is applied may occur, but such reactions are infrequent. Resistance to its tension-lowering effect may develop in some patients after several months. Retinal detachment has been reported in high myopia produced by isoflurophate, but the incidence appears to be no greater than that following the use of other commonly employed miotics. In case of accidental systemic administration, the concomitant injection of atropine sulfate to combat cholinergic action and magnesium sulfate to combat nicotinic action may be indicated; however, unless the systemic dose is sufficiently high to produce ganglionic paralysis, 0.4 to 0.6 mg. of atropine sulfate alone, parenterally, usually is adequate to overcome the parasympathomimetic effects of the drug in such emergencies.

Dosage.—Isoflurophate is administered locally in the eye by corneal instillation of a 0.1% solution in vegetable oil. The usual dosage is one to three drops of such solution in the affected eye every 8 to 72 hours. If possible, instillation should be made at night before retiring so that blurring of vision will be less disturbing.

Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of isoflurophate.

Meclizine Hydrochloride. — $C_{25}H_{27}ClN_2.2HCl$. — M.W. 463.87. — 1-(*p*-Chlorobenzhydryl)-4-(*m*-methylbenzyl)piperazine dihydrochloride.—The structural formula of meclizine hydrochloride may be represented as follows:



Actions and Uses.—Meclizine hydrochloride, like other antihistaminic agents, depresses the central nervous system. It exhibits a pronounced action against motion sickness as measured in human beings by a depressive effect upon the excitability of labyrinth and vestibular-cerebellar nerves. It is not yet clear whether such action can be explained by the interference with histamine (or a histamine-like substance), by the central depressant effect, or both. Pharmacological studies indicate that it has an antihistaminic potency at least as great as that of other similar agents and a somewhat longer duration of action. The action of a single oral dose is prolonged over a period of 9 to 24 hours.

Meclizine hydrochloride is effective in the prevention or treatment of motion sickness (including air sickness and seasickness) and in the treatment of nausea and vomiting associated with vertigo, labyrinthitis, Ménière's syndrome, and radiation sickness.

Meclizine hydrochloride, like other antihistamines, may produce drowsiness and other side-reactions, such as blurred vision, dryness of the mouth, and fatigue. Therefore, it should be used with caution by individuals whose activities require constant alertness in the operation of machinery, especially vehicles. Studies so far do not reveal that the drug is any more toxic than other similar agents, but until more is known of its long-term effects, physicians should be on guard for the appearance of untoward reactions. When prolonged use may be indicated, periodic blood cell counts should be made to detect any adverse effects on the hematopoietic system.

Dosage.—Meclizine hydrochloride is administered orally. An average oral dose for adults of 25 to 50 mg. once daily is recommended for the prevention of motion sickness. Ideally, the initial dose should be taken about one hour prior to embarkation to insure absorption (and retention) of the drug prior to the development of symptoms. Children require about one-half the adult dose. Similar oral dosage may be employed as tolerated in the treatment of radiation or motion sickness and for the control of nausea and vomiting in diseases involving the labyrinth or eighth cranial nerve.

Pfizer Laboratories, Division of Chas. Pfizer & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of meclizine hydrochloride.

Alseroxylon.—A fat-soluble alkaloidal fraction extracted from the root of Rauwolfia serpentina (Benth), containing reserpine and other nonadrenolytic amorphous alkaloids.

Actions and Uses.—Alseroxylon has the action of the sedative-antihypertensive-bradycrotic alkaloids of Rauwolfia serpentina, of which reserpine is among the most potent. It has the same uses and limitations as the whole root, rauwolfia, and its chief component alkaloid, reserpine. (See monograph on reserpine.)

Dosage.—Alseroxylon is administered orally. For adults the average oral dosage is 2 to 4 mg. daily. Higher oral dosage may be required for sedation of gross psychotic disturbances than for anxiety-tension syndromes associated with mild, labile hypertension or as an adjunct to more potent hypotensive agents in essential hypertension. (Orally, 1 mg. is approximately equivalent to 0.2 mg. of reserpine.)

Riker Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of alseroxylon.

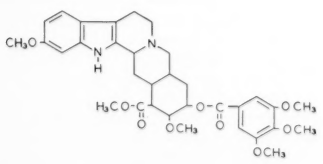
Rauwolfia.—The powdered whole root of Rauwolfia serpentina (Benth).

Actions and Uses.—Rauwolfia produces the sum of the actions of the total alkaloids contained in the whole root. The component alkaloids exhibit the sedative-antihypertensive-bradycrotic action characteristic of reserpine, the latter of which accounts for approximately 50% of their total activity. The whole root contains only insignificant amounts of yohimbine and other adrenolytic alkaloids. Thus, rauwolfia is useful for the same purposes and with the same precautions as for reserpine. See the monograph on reserpine.

Dosage.—Rauwolfia is administered orally. For adults the average oral dosage of the powdered whole root is 200 to 400 mg. daily, administered in two divided doses. Larger doses may be required for sedation of gross psychotic disturbances than for anxiety-tension states associated with mild, labile hypertension or as an adjunct to potent hypotensive agents in essential hypertension. Orally 200 to 300 mg. of powdered whole root is equivalent to 0.5 mg. of reserpine.

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of rauwolfia.

Reserpine.—$C_{33}H_{40}N_2O_9$.—M.W. 608.70.—An ester alkaloid isolated from the root of certain species of Rauwolfia. The structural formula of reserpine may be represented as follows:



Actions and Uses.—Reserpine is considered one of the most potent of the Rauwolfia alkaloids, which exhibit a sedative action and antihypertensive effect accompanied by bradycardia. Its antihypertensive effect is variable and ineffective in some patients. Studies in experimental animals indicate that the drug acts on the central nervous system, producing a tranquilizing nonhypnotic sedation, ptosis of the eyelids, sinus bradycardia, increased secretory and motor activity of the gastrointestinal tract, and a variable lowering of mean arterial blood pressure. The latter effect is attributed to a decrease in peripheral vasoconstriction apparently induced by central action on the vasomotor mechanism and is not associated with a significant alteration of cardiac output or renal plasma flow. Some effects of the drug suggest an action on the autonomic nervous system, although it does not exhibit either peripheral adrenolytic or peripheral parasympathomimetic activity and it does not block autonomic ganglions. Its observed effects are presumed to result from a central partial suppression of sympathetic predominance near the level of the hypothalamus where autonomic nervous functions are integrated. In contrast to barbiturates, reserpine produces less somnolence and does not alter significantly the electroencephalogram, depress the cortex, or prevent stimulant-induced convulsions.

The dose-response curve of reserpine is rather flat, although large doses may be associated with increased side-effects. After a single intravenous dose, the onset of sedative action of the drug usually occurs within about 30 minutes and the onset of antihypertensive effect usually begins within an hour. After intramuscular injection, the onset of these effects may appear slightly later in the same subjects. The maximum sedative and antihypertensive effect usually is reached within about 4 hours; the sedative action may persist longer (up to 12 hours) than the antihypertensive action (up to 10 hours) after intramuscular injection. The variations in time of onset and duration of action appear to be more a function of dosage and individual responsiveness than the route of parenteral administration. With daily oral administration the effects of the drug usually are not fully manifest for several days to 2 weeks and may persist for as long as 4 weeks after oral medication is discontinued. Tolerance to the drug does not develop with continued administration.

Reserpine is useful chiefly for its tranquilizing sedative action in the symptomatic management of patients with anxiety or tension psychoneuroses as such or as an accompaniment to somatic disorders and of patients with chronic psychoses involving anxiety, psychomotor hyperactivity, or compulsive aggressive behavior. It is useful also for the management of mild, labile hypertension associated with anxiety and emotional factors and, in conjunction with potent hypotensive agents, for the management of essential hypertension and hypertension associated with toxemia of pregnancy. The use of reserpine alone is considered to be of little value for severe or fixed hypertension, but it is useful to enhance or prolong the action of potent hypotensive agents to reduce dosage and side-effects. It probably should not be used with barbiturates in eclampsia or other conditions in which profound sedation would be undesirable. The value of reserpine for routine use as a prophylactic against progressive vascular changes in patients with early hypertension has not been established. The exclu-

sive use of reserpine in severe hypertension also may be considered dangerous because it may create a false sense of security at the expense of more effective measures.

Higher doses of the drug (administered orally and parenterally) usually are required in the management of grossly disturbed psychoses than in anxiety-tension states where the oral route usually is adequate. In both types of patients the drug must be administered for a period of 1 (usually) or 2 weeks before the optimal level of dosage can be determined. The tranquilizing effect of the drug may make the psychotic patient more accessible for concurrent psychotherapy; however, in the treatment of very disturbed psychotic patients, the effect of the drug should be carefully observed to avoid the development of an oblique attitude of indifference or detachment toward the underlying emotional conflicts. It should be realized that unless dosage is carefully adjusted the drug may induce a paradoxical form of anxiety and an adverse reactive depression. In chronic psychoses the drug does not appear to alter the basic psychopathological state.

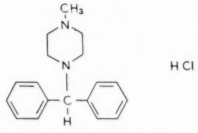
Reserpine has a rather low toxicity but may be associated with undesirable or toxic side-effects especially at the high dosage levels. Side-effects are more likely to occur in hypertension when the dosage of the drug, which does not have a pronounced antihypertensive effect, is increased in an effort to obtain a greater response. The side-effects commonly include nasal stuffiness, weight gain, and diarrhea and, less frequently, dryness of the mouth, insomnia, nervousness, paradoxical anxiety, increased gastrointestinal activity, chronic fatigue or sense of weakness in the extremities, muscular aching, nightmares, and agitated or paranoid depression. Skin eruptions occur rarely and peptic ulceration is a rare complication. Epistaxis also has been encountered. A paralysis agitans-like syndrome has been observed; this is reversible and apparently results from excessive dosage. Postural hypotension may occur occasionally after parenteral administration, but this rarely occurs after oral administration except with large dosage.

Parenteral therapy with reserpine alone is indicated in mild hypertension only when oral administration is not feasible. When relatively large doses are required, as in chronic psychoses, intramuscular injection is indicated in conjunction with oral medication; oral administration is best suited for use in conjunction with potent hypotensive drugs in chronic, severe hypertension. Because of the slow and variable antihypertensive effect, parenteral injection of reserpine alone is not suitable for the management of hypertensive crises.

Dosage.—Reserpine is administered orally and by intramuscular or intravenous injection. The usual oral dosage for adults in the treatment of mild, labile hypertension is 0.25 to 1 mg. daily in two or three divided doses. In some cases as little as 0.05 mg. or as much as 1.5 mg. daily may be required. As an adjunct to more potent hypotensive agents in severe hypertension, 0.25 to 0.5 mg. daily is usually adequate. In anxiety or tension psychoneuroses, the daily dosage is 0.5 to 2 mg. In disturbed psychotics an oral dosage of 3 to 5 mg. daily is usually employed in conjunction with intramuscular injection of 5 to 10 mg. daily, depending on the response to the drug.

Ciba Pharmaceutical Products, Inc., Eli Lilly & Company, Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., and Riker Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of reserpine.

Cyclizine Hydrochloride. — $C_{18}H_{22}N_2.HCl$. — M.W. 302.86. — 1-diphenylmethyl-4-methylpiperazine hydrochloride.—1-benzhydryl-4-methylpiperazine hydrochloride.—The structural formula of cyclizine hydrochloride may be represented as follows:



Actions and Uses.—Cyclizine hydrochloride is an antihistamine compound that has been found useful in the prevention and relief of motion sickness. Its usefulness as a histamine antagonist in allergic states has not been evaluated. The drug appears to be effective in the control of vertigo, nausea, and vomiting in a high percentage of cases of seasickness and airsickness. Like certain other antihistamines, cyclizine also appears to reduce sensitivity of the labyrinth in the symptomatic relief of vertigo and concomitant symptoms caused by vestibular disorders. The use of the drug for this purpose should not be continued longer than a week without determining the presence or absence of serious vestibular disease or toxic sources of vestibular disturbance for which corrective treatment may be indicated. Its effectiveness for the prevention or treatment of nausea and vomiting from other causes, such as pregnancy and after surgery and anesthesia, has not been established.

In doses ordinarily effective against motion sickness, cyclizine hydrochloride appears to be relatively free of the side-effects usually encountered with antihistamine drugs. High dosage may cause some drowsiness and mouth dryness. The possibility of sedation also should be kept in mind when the drug is used in susceptible persons operating vehicles or machines that require constant alertness.

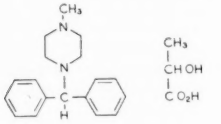
Dosage.—Cyclizine hydrochloride is administered orally. To prevent and relieve motion sickness, the usual dosage for adults is 50 mg. one-half hour before departure and 50 mg. three times daily before meals. Continued administration of the drug may be unnecessary after the first 2 or 3 days of extended travel, depending on the type of travel, duration of the trip, and susceptibility of a person to motion sickness.

To relieve vertigo and concomitant symptoms of vestibular disorders, the minimum oral dosage for adults is 50 mg. three times daily; twice this amount may be required to completely relieve symptoms.

One-half the adult dosage is suggested for children 6 to 10 years, and one-fourth the adult dosage for those under 6 years of age.

Burroughs Wellcome & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of cyclizine hydrochloride.

Cyclizine Lactate.—$C_{18}H_{22}N_2.C_3H_6O_3$.—M.W. 355.46.—1-diphenylmethyl-4-methylpiperazine lactate.—1-benzhydryl-4-methylpiperazine lactate.—The structural formula of cyclizine lactate may be represented as follows:

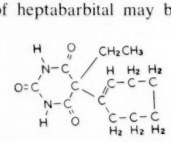


Actions and Uses.—Cyclizine lactate has the same systemic actions as the hydrochloride salt of the drug. (See monograph on cyclizine hydrochloride.) The lactate is suitable for intramuscular injection when the oral route is not feasible for the control of motion sickness or vertigo caused by other vestibular disturbances. Its usefulness for the prevention or treatment of nausea and vomiting from other causes has not been established.

Dosage.—Cyclizine lactate is administered by intramuscular injection in a solution containing 50 mg. per cubic centimeter. The dosage is the same as for the orally administered hydrochloride. (See monograph on cyclizine hydrochloride.)

Burroughs Wellcome & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of cyclizine lactate.

Heptabarbital.—$C_{13}H_{18}O_3$.—M.W. 222.29.—5-(1-cyclohepten-1-yl)-5-ethylbarbituric acid.—The structural formula of heptabarbital may be represented as follows:



Action and Uses.—Heptabarbital is qualitatively similar in action to other short-acting, chemically related barbiturates. It produces sedation, hypnosis, or anesthesia, depending on the dose administered, but has not been demonstrated to have specific analgesic properties. It exerts a mild spasmolytic effect on smooth muscle and produces mild hypotension as a result of central sedation and peripheral vasodilation. Low grade tolerance develops readily with repeated administration, but this does not appear to be greater than that observed with other barbiturates. Euphoria may accompany the use of fairly large doses, and, like other short-acting barbiturates, the drug is potentially capable of inducing habituation and physical dependence.

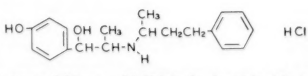
Heptabarbital appears to be readily absorbed from the gastrointestinal tract and undergoes rapid metabolic destruction in the body. The latter characteristic probably accounts for its short duration of action and relative lack of cumulative effects. Biochemical studies indicate that the compound first is oxidized to a ketone, which then undergoes such rapid further degradation that less than 4% of the ketone can be recovered in the urine; none of the drug is excreted unchanged. Whereas the experimental and some clinical studies demonstrate that heptabarbital accumulation in the body is less than with pentobarbital, this represents only a theoretical clinical advantage and does not take into consideration individual variations in the detoxication capacity of the liver or other organs.

Heptabarbital is worthy of clinical trial as a comparatively short-acting barbiturate in all situations for which mild sedation or hypnotic action is indicated. Its use as an anesthetic agent has not been adequately explored. At the hypnotic dosage level its acute toxicity is about one-third that of pentobarbital, 0.6 gm. of heptabarbital being roughly equivalent to 0.2 gm. of pentobarbital. A single hypnotic oral dose of 0.2 to 0.4 gm. of heptabarbital, given 30 to 45 minutes before retiring, rarely is associated with "hangover." A minimum of side-effects has been observed after daily doses of 0.6 to 2.4 gm.; gastrointestinal disturbances, skin eruption, excitement, or other side-effects are rarely encountered. Chronic toxicity studies in dogs receiving 100 mg. per kilogram of body weight per day for 90 days have revealed no unusual biochemical changes and no evidence of injury to the parenchymatous tissues or the blood-forming organs. Until longer clinical experience with the drug indicates otherwise, however, it should be employed with the general precautions applicable to all barbiturates.

Dosage.—Heptabarbital is administered orally. The optimal effective dosage has not been conclusively established. For sedation, 50 to 100 mg. two or three times daily is suggested. The suggested hypnotic dose is 0.2 to 0.4 gm. before retiring. Some patients may require a hypnotic dose of 0.6 gm. Until the effective dosage is more firmly established, it may be preferable to start with the suggested lower amounts, adding moderate daily increments until a satisfactory level of sedation or hypnosis is obtained.

Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of heptabarbital.

Nylidrin Hydrochloride.—$C_{19}H_{25}NO_2.HCl$.—M.W. 345.88.—1-(*p*-hydroxyphenyl)-2-(1-methyl-3-phenylpropylamino)propanol hydrochloride.—The structural formula of nylidrin hydrochloride may be represented as follows:



Actions and Uses.—Nylidrin hydrochloride is an epinephrine-ephedrine type of compound that acts as a peripheral vasodilator. The site of action is the same as that of other sympathomimetic drugs, but its effect is vasodilator only, producing relaxation of the muscle fibers in the media of the vessel wall. Its action appears to be almost selective upon the small arteries and arterioles of skeletal muscle. It increases muscle blood flow but has little or no effect upon the superficial skin vessels. This action upon the vessels of skeletal muscle has been demonstrated in both human and animal experiments. Studies with plethysmographic measurements have confirmed the ability of nylidrin hydrochloride to increase muscle blood flow and to exercise tolerance in peripheral vascular disease.

The activity of nylidrin hydrochloride results in the mobilization of depot blood and brings about an increased cardiac output. In the hypertensive individual the mean arterial pressure may drop, whereas in the hypotensive patient the mean arterial pressure may actually increase, in comparison to the sitting normotensive individual in whom the mean arterial pressure is either unaltered or only slightly diminished. The drug is rapidly absorbed from the gastrointestinal tract and is only slightly affected by digestive enzymes. It is slowly metabolized and has a protracted action.

Nylidrin hydrochloride is indicated in vascular disorders of the extremities that may be benefited as the result of increased blood flow. Accordingly, it is worthy of trial in intermittent claudication and Raynaud's disease and as an adjunct to other measures in severe forms of peripheral vascular disease such as diabetic vascular disease, thrombophlebitis, thromboangiitis obliterans, ischemic ulcers, and endarteritis obliterans. Minor side-effects such as nervousness or palpitation may occur, but usually these are transient and disappear with continued therapy or reduction of dosage. The drug should be used with caution in hyperthyroidism, paroxysmal tachycardia, and severe angina pectoris. It is contraindicated in acute coronary thrombosis.

Dosage.—The suggested initial dosage for adults is 6 mg. orally three times daily. This may be increased to four to six times daily, depending upon clinical response and individual tolerance. If side-effects develop and persist, the dose should be reduced to 3 mg. three times daily or therapy temporarily discontinued and then resumed with lower doses.

Arlington-Funk Laboratories, Division of U. S. Vitamin Corporation, cooperated by furnishing scientific data to aid in the evaluation of nylidrin hydrochloride.

Sodium Radio-Chromate (Cr^{51}).—Anionic hexavalent radioactive chromium (Cr^{51}) in the form of sodium chromate ($Na_2Cr^{51}O_4$). The radio-chromium (Cr^{51}) has a half-life of 26.5 days. It disintegrates primarily by K capture, with transmutation to vanadium and emission of x-rays.

Actions and Uses.—The presence of a gamma ray of 0.32 mev energy in the radiation emitted by radio-chromium makes sodium radio-chromate (Cr^{51}) useful as a biological tracer. When mixed with whole blood, the hexavalent chromate anion (CrO_4--) readily diffuses through the wall of the red blood cells and inside the cells is reduced to the trivalent chromic cation ($Cr+++$), which then firmly associates with the globin portion of their contents. Because the chromic form of the isotope apparently is not capable of passing the cell wall barrier and thus cannot be reutilized by intact cells, erythrocytes can be tagged by exposure to the diffusible chromate anion for determinations of circulating red cell volume and studies of red cell survival time. The isotope also can be employed for the determination of whole blood volume (red cell mass and plasma volume), used either alone or in conjunction with radioactive chromic chloride ($Cr^{51}Cl_3$). The radioactive chromic cation released by destruction of tagged erythrocytes readily combines with plasma proteins; however, the radioactivity of the plasma is lost more rapidly than that of the cells so that neither form of the isotope interferes with the other when used alone or simultaneously for such studies.

To tag erythrocytes, a sample of the patient's blood or of donor blood is mixed with a solution of sodium radio-chromate (Cr^{51}) and allowed to stand until the isotope diffuses into the cells. The unbound chromium (in the plasma) is then either reduced by addition of ascorbic acid or removed by separation and washing of the cells. The treated blood or a suspension of the separated cells is then injected into the circulation, and sufficient time is allowed for complete in vivo mixing before samples are taken for scintillation counting. Red cell or whole blood volume is estimated by the radioisotope dilution method. Red cell survival time may be studied by a similar technique with samples taken at appropriate intervals and corrections made for decay in gamma radiation. Consistently lower values for whole blood volume are obtained by the radioactive chromium method than by the dye method. Normal mean values for whole blood volume obtained by the isotope method are 65.6 ± 5.95 cc. per kilogram of body weight, or 2.49 ± 0.28 liters per square meter of body surface.

Sodium radio-chromate (Cr^{51}) has not been shown to produce any significantly deleterious effects on normal erythrocytes, either from the standpoint of radioactivity or the amount of metallic chromium present. Because the bond that is formed with the cells is stable, the isotope has the advantage of permitting leisurely conducted radioisotopic studies of erythrocytes, including rechecks up to 24 hours, without correcting for loss of radioactivity. In studying red cell survival it eliminates the necessity for using donor cells and thus is free from the danger of incompatibilities of blood type or of transmission of the virus of serum hepatitis.

Dosage.—Sodium radio-chromate (Cr^{51}) is used in the form of a solution suitable for intravenous injection that first is mixed with a sample of 40 or 50 cc. of whole blood withdrawn from the patient or from a compatible donor. The dose is based upon the amount necessary to tag 80 to 90% of the erythrocytes in the sample of whole blood and ranges from 75 to 125 μc (microcuries) with conventional techniques. Doses as low as 10 to 15 μc have been used with special techniques for determinations of whole blood volume. After it is mixed with the appropriate dose, the sample should be allowed to stand for 15 to 60 minutes to achieve adequate tagging. After appropriate reduction or removal of the unbound portion of the isotope, the treated sample or separated suspension of erythrocytes is then injected and allowed to mix with the circulating blood before samples are withdrawn for counting.

As the tagged cells are very stable, repeat doses are seldom indicated. In conditions such as severe hemolytic anemia where red blood cell survival studies may be indicated before, during, and after treatment, and where repeat doses are necessary because of rapid destruction of red blood cells, the number of repeat doses should be kept at a minimum and the total dosage should not exceed 390 μc in the body at any one time.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of sodium radio-chromate (Cr^{51}).

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The following article was prepared at the request of the Council on Foods and Nutrition.

EUGENE H. STEVENSON, M.S.
Acting Secretary.

VITAMIN B_6 IN MEDICAL PRACTICE

Richard W. Vilter, M.D., Cincinnati

Whenever a new vitamin or an altered form of an existing one is added to the medical armamentarium, it is received with such enthusiasm that for a time it appears to be a panacea for human ills. Usually, after a number of years, the test of time and further research demonstrate its area of real value. Such was the story with thiamine, ascorbic acid, folic acid, and cyanocobalamin (vitamin B_{12}). With vitamin B_6 there have been two surges of enthusiasm, one just after it was synthesized by Harris and Folkers in 1939 and another going on now and based on much more complete and convincing data. Thus it seems desirable to pause and evaluate the present position of vitamin B_6 in therapy.

Vitamin B_6 is, in reality, a group of closely related chemical compounds that may be called the vitamin B_6 complex. Pyridoxine [2-methyl-3-hydroxy-4,5-di-(hydroxymethyl) pyridine] is found primarily in the vegetable kingdom. If the 4-hydroxymethyl group is oxidized to an aldehyde, pyridoxal is formed. If the hydroxy group is replaced by an amino group, the result is pyridoxamine. Both pyridoxal and pyridoxamine occur primarily in the animal kingdom and exist as phosphates, this radical being attached to the 5-hydroxymethyl group. Thus pyridoxal phosphate seems to exist in equilibrium with pyridoxamine phosphate. The active coenzyme form of the vitamin is usually considered to be 5-pyridoxal phosphate.

The members of the vitamin B_6 group may be oxidized still further to pyridoxic acid, the chief excretory product of B_6 found in the urine. This form of the vitamin is metabolically inactive. Metabolic antagonists for vitamin B_6 have been synthesized, the one most commonly used in research being 4-desoxypyridoxine. As the name implies, the oxygen atom has been removed from the 4-methylhydroxy group, leaving a methyl group in its place. When this substance is phosphorylated, cells apparently mistake it for pyridoxal phosphate, but, being inactive, it inactivates the enzyme systems to which it attaches.

Vitamin B_6 is so widely distributed in nature that only under unusual circumstances is it possible for a dietary deficiency state to occur. Much more accurate data are needed on the vitamin B_6 content of many foods, but enough information is available to support this statement. When human beings take vitamin B_6 by mouth, it appears to be absorbed very readily from the gastrointestinal tract, pyridoxal more rapidly than pyridoxine or pyridoxamine, as indicated by a greater and more rapid excretion of pyridoxic acid in the urine. A considerable amount of the vitamin is present in the feces, but this is derived, apparently, from intestinal microorganisms. Whether any of this fecal vitamin B_6 is absorbed by the human being cannot be answered as yet. Meager evidence so far is against much absorption from this source; however, laboratory animals such as the rat do obtain some vitamin B_6 in this way. A small amount of vitamin B_6 appears in the urine as pyridoxal and pyridoxamine. A much larger amount appears as pyridoxic acid. Since the test for pyridoxic acid measures other fluorescent substances as well, it is unreliable at low levels and, in persons on a normal diet, indicates a greater day-to-day excretion of pyridoxic acid than actually occurs.

The daily requirement of vitamin B_6 for human beings is estimated to be 1 to 2 mg.; the average American diet provides this much with ease. The average amount of vitamin B_6 lost in the stool is 0.5 to 0.8 mg. The average amount lost in the urine as the active vitamin is 0.2 to 0.3 mg. and as pyridoxic acid 3 to 4 mg. In order to bring these data into balance, one must remember that the vitamin lost in the stool has been derived primarily from micro-organisms and does not represent food vitamin B_6 and that the pyridoxic acid values are erroneously high. It is probable that a balance occurs at an intake-output of about 2 mg. Very little vitamin B_6 is found in the blood. Serum levels average about 5 mcg. per 100 cc. Pyridoxal phosphate levels are even lower. Tissue levels have not been determined often enough in human beings for a statement of values, though the level for normal skin appears to be about 1 mcg. per gram (dry weight).

Within the cells, vitamin B_6 performs many extremely important functions. When pyridoxal phosphate is combined with specific protein enzymes, it can act as a transaminase, decarboxylase, and desulfurase; that is, it can catalyze the transfer of amino groups from an amino acid to a keto acid to form a new amino acid, it can remove a carboxyl group from amino acids, and it can remove sulfhydryl groups from sulfur-containing compounds. All of these are reversible reactions. In these ways, vitamin B_6 provides raw materials for the Krebs cycle, one of the most important energy sources in the body; builds up new amino acids; and transfers sulfhydryl groups from one compound to another. It is important also for tryptophan metabolism, particularly for the conversion of tryptophan to nicotinic acid derivatives, and for the interconversion of the essential fatty acids.[1] The metabolic antagonist of B_6, desoxypyridoxine, has been shown to block most of these reactions; desulfuration is unaffected.

DEFICIENCY

Chemical tests for vitamin B_6 deficiency in human beings are based on alterations of the physiology and biochemistry just described. A urine vitamin B_6 level under 100 mcg. per 24 hours as measured by growth of

From the Department of Internal Medicine, University of Cincinnati, College of Medicine.

1. Snell, E. E.: Summary of Known Metabolic Functions of Nicotinic Acid, Riboflavin and Vitamin B_6, Physiol. Rev. 33: 509 (Oct.) 1953.

the yeast Saccharomyces carlsbergensis is presumptive evidence of deficiency. The pyridoxic acid excretion cannot be determined with sufficient accuracy at low levels to make this a satisfactory test for deficiency states; however, it will measure the excretion of pyridoxine or pyridoxal administered as a load test and will detect reduced excretion (and therefore presumably increased storage) in persons whose tissues have become unsaturated during a period of deficiency. A test load of 25 mg. of crystalline pyridoxal has been recommended. Pyridoxic acid is measured in a four or eight hour collection of urine. A normal excretion of about 50% of the administered vitamin as pyridoxic acid is expected. Even in normal persons vitamin B_6 levels in blood and tissues are at the lower limits of accuracy of the test, so that these methods are unsatisfactory for the study of deficiency states.

A much simpler and more satisfactory method depends upon the appearance of an abnormal metabolite of tryptophan, xanthurenic acid, in the urine in persons who have become deficient in vitamin B_6. In order to bring out this defect, a *dl* tryptophan load of 10 gm. must be administered and the urine collected for 24 hours thereafter and analyzed for xanthurenic acid. Values over 50 mg. are abnormal and can be reduced by extra pyridoxine. A physiological test that is somewhat more complex depends upon delayed utilization of amino nitrogen in vitamin B_6-deficient human beings and animals. After a load of 30 gm. of alanine, the urea nitrogen level should return to normal in a shorter time than 12 hours. In vitamin B_6 deficient subjects, this clearing effect is delayed and blood urea nitrogen levels remain elevated longer than 12 hours.

Studies.—Vitamin B_6 deficiency has been studied in human beings in three ways: (1) by elimination of the vitamin from the diet, a method that requires a synthetic ration; (2) by counteracting the effect of the vitamin with an antivitamin such as 4-desoxypyridoxine; and (3) by administering the vitamin as a therapeutic test in numerous diseases, some related, others unrelated, to dietary deficiency.

In 1950 Snyderman and his associates [2] studied two hydrocephalic infants maintained on a synthetic diet devoid of vitamin B_6. After 76 days, convulsions developed in one of these infants; after 130 days, anemia developed in the other. Both excreted large amounts of xanthurenic acid in the urine after a load test of tryptophan and failed to excrete a normal amount of N^1-methyl-nicotinamide. All of these abnormalities disappeared after pyridoxine was administered, the N^1-methyl-nicotinamide excretion being the last to return to normal. Greenberg and others [3] maintained two adult subjects on a vitamin B_6 deficient diet for three weeks. Although the period was too short for the development of symptoms and signs, excessive amounts of xanthurenic acid appeared in the urine after a tryptophan load. In another attempt, one subject was maintained on a vitamin B_6 deficient diet for 54 days, but no manifestations of deficiency disease developed.

Vilter and associates [4] studied the problem of vitamin B_6 deficiency in 50 volunteer patients with the aid of the metabolic antagonist 4-desoxypyridoxine. Some were maintained on a vitamin B_6 deficient diet, and others were given a normal hospital diet. The deficiency state developed more rapidly in those on the deficient regimen but occurred in both groups. It could be reversed completely by pyridoxine or its relatives and reversed partially by the essential fatty acid linoleic acid. Many of the patients became irritable, depressed, and sometimes somnolent. Others were not affected mentally. Seborrheic dermatitis developed in the nasolabial fold, in the eyebrows, and around the eyes in 29 of the patients. It spread over the face, forehead, and chin, up into the hair, and down the neck. In several persons it involved the perineal region also. Intertrigo developed under the breasts and in the groin in several women, and occasionally a hyperpigmented, scaling, pellagrous-like dermatitis developed on the arms and legs. Cheilosis, angular stomatitis, and conjunctivitis developed in six. Glossitis was noted in 14, and peripheral neuritis was a prominent feature in 3. Lymphopenia occurred regularly, but anemia that occurred could not be related to the vitamin B_6 deficiency state. After tryptophan was administered, large amounts of xanthurenic acid appeared in the urine. Urea nitrogen levels were elevated and, after the administration of alanine, remained so for longer than 12 hours. All these abnormalities were relieved by administration of the members of the vitamin B_6 group but were not influenced by thiamine, niacin, or riboflavin. Linoleic acid relieved the skin lesions but had no effect on the other clinical or laboratory features. This study indicates that vitamin B_6 deficiency in human beings is not very different from the syndrome observed in laboratory animals and also indicates that it encompasses all the features of mixed vitamin B complex deficiency disease.

Incidence.—Although it seems probable that vitamin B_6 deficiency disease is very rare because of the presence of this nutrient in many common foodstuffs, the deficiency state would be difficult to recognize since it mimics so closely other vitamin B complex deficiency diseases. However, there is evidence that it does exist under special circumstances. In 1939, Spies and others [5] reported that patients with mixed vitamin B complex deficiency disease who had been treated with nicotinic acid, riboflavin, and thiamine remained weak, nervous, irritable, and sleepless until they received pyridoxine. Muscle weakness as demonstrated by ergographic records was noted in pellagrins in Egypt by Hammouda and Sidky.[6] This weakness was not relieved by nicotinic acid but was by pyridoxine; however, I was unable to find chemical evidence of vitamin B_6 deficiency in Egyptian pellagrins.

In 1939, Smith and Martin [7] reported that pyridoxine was effective in healing cheilosis and angular stomatitis

2. Snyderman, S. E.; Holt, L. E., Jr.; Carretero, R., and Jacobs, K.: Pyridoxine Deficiency in the Human Infant, J. Clin. Nutrition **1**: 200 (March-April) 1953.

3. Greenberg, L. D.; Bohr, D. F.; McGrath, H., and Rinehart, J. F.: Xanthurenic Acid Excretion in the Human Subject on a Pyridoxine-Deficient Diet, Arch. Biochem. **21**: 237 (March) 1949.

4. Vilter, R. W., and others: The Effect of Vitamin B_6 Deficiency Induced by Desoxypyridoxine in Human Beings, J. Lab. & Clin. Med. **42**: 335 (Sept.) 1953.

5. Spies, T. D.; Bean, W. B., and Ashe, W. F.: A Note on the Use of Vitamin B_6 in Human Nutrition, J. A. M. A. **112**: 2414 (June 10) 1939.

6. Hammouda, M., and Sidky, M.: Pyridoxine, an Essential Factor in the Restoration of Muscle Power of Egyptian Pellagrins, J. Roy. Egyptian M. A. **35**: 413, 1952.

7. Smith, S. G., and Martin, D. W.: Cheilosis Successfully Treated with Synthetic Vitamin B_6, Proc. Soc. Exper. Biol. & Med. **43**: 660 (April) 1940.

that did not respond to riboflavin. Much more convincing evidence that pyridoxine deficiency can occur in infants under natural conditions was inadvertently produced when a commercial liquid milk product was processed in such a way that the vitamin B_6 content was reduced to about 60 mcg. per liter. At the same time, the source of fatty acids was changed. Apparently as a result of either one or both of these maneuvers, convulsive seizures occurred in many infants who were fed this product.[8] In all, 60 infants between the ages of 2 and 4 months were observed in two studies. Convulsive seizures were accompanied by rapid pulse, gasping respirations, and abnormal color, and electroencephalograms were abnormal. In most of the infants, dietary change alone was sufficient to relieve the convulsions. In one infant, an intramuscular dose of 100 mg. of pyridoxine relieved the convulsions and restored the electroencephalographic pattern to normal in five minutes.

About this same time Hunt and others[9] studied an infant with convulsive seizures. This child was born of a mother who had had much pyridoxine administered during her pregnancy for recurring vomiting. A sibling had died of convulsions shortly after birth. The convulsions of the child studied ceased when a mixed vitamin B complex preparation was administered, only to begin again when it was discontinued. Hunt found that pyridoxine was the active material in the vitamin B complex preparation. At last report, the child was doing well as long as several milligrams of pyridoxine were administered daily. In this case, it was clear that a true deficiency state did not exist. Xanthurenic acid output after a tryptophan load test was normal. For some unknown reason, this child had an unusually high vitamin B_6 requirement, particularly for normal central nervous system function. Thus far, this is the only example of such a condition.

ISONIAZID AND VITAMIN B_6

In 1954, Biehl and Vilter[10] were able to prevent neuritis that occurred in patients who received large doses of isoniazid (N-isonicotinylhydrazine, INH) by giving pyridoxine concurrently. Neuritis developed in 2 to 3% of patients receiving conventional doses of isoniazid (2 to 3 mg. per kilogram of body weight), whereas this abnormality developed in 40% of patients receiving 20 mg. per kilogram of body weight. For prophylaxis, 50 mg. of pyridoxine daily was sufficient. When this work was begun, these investigators were aware that isoniazid inactivated certain decarboxylase enzyme systems that required pyridoxal phosphate as coenzyme and that peripheral neuritis occurred rarely in persons with vitamin B_6 deficiency induced by 4-desoxypyridoxine. They were able to show that increasingly large doses of isoniazid increased the amount of pyridoxal, but not of pyridoxic acid found in the urine and that xanthurenic acid excretion increased after administration of tryptophan, but in an irregular fashion. These investigators propose that isoniazid may couple with pyridoxal to form a pyridoxal isoniazid hydrazone, thus inactivating enzyme systems dependent on pyridoxal and causing large amounts of a hydrolyzable vitamin B_6 compound to appear in the urine. In this manner a conditioned vitamin B_6 deficiency state might be induced.

Recently, a relationship between isoniazid and vitamin B_6 insufficiency has been established in rats.[11] In an Escherichia coli mutant, isoniazid has been shown to inactivate tryptophanase by blocking the entrance of pyridoxal phosphate into the molecule. It does not appear at present that isoniazid inhibits the growth of tubercle bacilli in this fashion, nor that moderate doses of vitamin B_6 interfere with the antituberculous effect of isoniazid.

THERAPEUTIC USE

Pyridoxine or other B_6 vitamins have been used in many conditions that, because of clinical similarities to natural or induced vitamin B_6 deficiency, have encouraged the investigator to perform a therapeutic trial. In a few cases the evidence of benefit is good; in most, it is nebulous.

Because vitamin B_6 deficiency in animals and human infants is characterized by a convulsive disorder, this vitamin has been tried in various doses in epilepsy. Fox and Tullidge[12] did not observe any beneficial effects when the dose administered ranged from 20 to 120 mg. daily for several weeks. Ernsting and Ferwerda,[13] however, in a less carefully controlled series of cases, reported some degree of benefit. More recent work does not support the use of vitamin B_6 as an agent of therapeutic value in most cases of epilepsy, yet there is suggestive evidence that it may have an indirect effect on the metabolic defects that may lead to these convulsive seizures. The elucidation of these relationships must await careful metabolic studies of the future.

Vitamin B_6 has been evaluated as a therapeutic agent in patients with arteriosclerotic and postencephalitic Parkinsonism and in persons with progressive muscular atrophy, amyotrophic lateral sclerosis, and muscular dystrophy. These reports have been reviewed adequately in a previous article on vitamin B_6 in THE JOURNAL.[14] Most of the evidence does not support the therapeutic claims that have been advanced, although apparently a few patients, particularly those with arteriosclerotic Parkinsonism, have been benefited. This field is so beclouded by subjective responses unsupported by objective evidence of improvement that no judgment can be made. In general, these diseases continue to follow their progressive downhill course despite the availability of vitamin B_6 for the past 15 years.

Reports of beneficial effects of vitamin B_6 on various neuritides are also scattered through the medical literature, but these too lack confirmation. It is possible that,

8. May, C. D.: Vitamin B_6 in Human Nutrition: A Critique and an Object Lesson, Proc. Inst. Med. Chicago **20**: 83 (April) 1954.

9. Hunt, A. D., Jr.; Stokes, J., Jr.; McCrory, W. W., and Stroud, H. H.: Pyridoxine Dependency: Report of a Case of Intractable Convulsions in an Infant Controlled by Pyridoxine, Pediatrics **13**: 140 (Feb.) 1954.

10. Biehl, J. P., and Vilter, R. W.: Effect of Isoniazid on Vitamin B_6 Metabolism: Its Possible Significance in Producing Isoniazid Neuritis, Proc. Soc. Exper. Biol. & Med. **85**: 389 (March) 1954.

11. Rosen, F.: Effect of Isonicotinic Acid Hydrazide on Niacin and Pyridoxine Metabolism in Rats, Proc. Soc. Exper. Biol. & Med. **88**: 243 (Feb.) 1955.

12. Fox, J. T., and Tullidge, G. M.: Pyridoxine (Vitamin B_6) in Epilepsy: A Clinical Trial, Lancet **2**: 345 (Sept. 7) 1946.

13. Ernsting, W., and Ferwerda, T. P.: Vitamin B_6 (Pyridoxine, Adermine) in Therapy of Epilepsy, Nederl. tijdschr. geneesk. **95**: 3643 (Dec. 8) 1951.

14. Pyridoxine Hydrochloride (Vitamin B_6): A Status Report, report of the Council on Pharmacy and Chemistry, J. A. M. A. **147**: 322 (Sept. 22) 1951.

in this field, as in that of epilepsy, future investigations may show that vitamin B_6 sometimes induces improvement by activating alternate metabolic pathways, thus circumventing a biochemical defect that as yet has not been discovered. At this time, however, vitamin B_6 cannot be considered to be effective therapy for any of these conditions.

There are also several reports that pyridoxine has had a beneficial effect on granulocytopenia resulting from drug toxicity and x-ray irradiation; however, use of the damaging drugs was discontinued when administration of pyridoxine was begun, and the course of the patients was such as might have been expected with good supportive treatment alone. Furthermore, vitamin B_6 deficiency in animals has caused neutrophilic leukocytosis, and addition of the vitamin has reduced the leukocyte count. There is no experimental evidence of a stimulating effect of vitamin B_6 on any white blood cell except the lymphocyte. Scattered through the medical literature, one can find reports of beneficial effects of vitamin B_6 on acute and chronic alcoholism and senile involution. The enthusiasm of the investigators, rather than the vitamin B_6 that was administered, was likely responsible for the favorable effects.

Schreiner and his associates [15] noted the morphological and histological similarity of the seborrhea-like lesions that appeared in patients with seborrheic dermatitis of natural origin treated with 4-desoxypyridoxine. There were previous reports that pyridoxine administered orally or parenterally brought about improvement in such skin lesions and in acne as well. Schreiner and his associates were unable to demonstrate any improvement in seborrheic dermatitis of spontaneous origin when pyridoxine was administered orally or parenterally, but, when a cream containing 1 or 2% pyridoxine was applied to the natural lesion, they noted improvement within one to two weeks. The cream alone did not have this effect, and, after use of the pyridoxine cream was discontinued, relapse occurred in most cases within one month. Xanthurenic acid excretion after a tryptophan load test was within normal limits in these patients. In several, sharp differentiation could be made between the effect of the cream alone applied to one side of the face and that of the cream containing 1% pyridoxine applied to the other side. Only the dry type of seborrhea appeared to respond. These observations have not been confirmed by Effersoe,[16] who found that the cream alone induced as much improvement as the cream containing pyridoxine. Both preparations decreased sebum production; therefore, the relationship of vitamin B_6 to spontaneous seborrheic dermatitis is still in doubt.

For many years pyridoxine has been used empirically in women with nausea and vomiting of pregnancy and in persons who vomited after heavy doses of x-ray irradiation or after anesthesia. Only recently, a physiological abnormality involving vitamin B_6 has been demonstrated in the pregnant woman. Wachstein and Gudaitis [17] have shown that pregnant women in the second and third trimester given a test dose of tryptophan excrete abnormally large amounts of xanthurenic acid in the urine when compared with nonpregnant women and that this abnormality is quickly relieved by pyridoxine in doses of 25 mg. daily. They have also shown a small but statistically significant difference between the amount of 4-pyridoxic acid that appears in the urine of pregnant and the amount appearing in the urine of nonpregnant women after a load test with 25 mg. of pyridoxine. McGanity and his associates [18] have demonstrated that pregnant women have lower blood urea nitrogen levels on the average than do nonpregnant women, the lowest levels occurring in women with hyperemesis gravidarum. They showed also that, after a test dose of alanine, the blood urea nitrogen level remained elevated for more than 12 hours in women with hyperemesis gravidarum, whereas it returned to normal levels after this length of time in nonpregnant women. Therefore, it appears that there may be some physiological basis for a practice that had its roots in empiricism but has never been carefully enough controlled to be established as an accepted therapeutic procedure. A double-blind therapeutic trial is still needed badly, however, since there is still no evidence that the metabolic abnormalities of the pregnant woman that are rectified by pyridoxine have any relationship to the nausea and vomiting from which she suffers. Neither is it clear that an actual deficiency of pyridoxine exists. The problem may be a greater than normal need for pyridoxine in certain biochemical reactions related to tryptophan and other amino acids.

There is no supportive experimental evidence regarding the use of pyridoxine in postanesthetic nausea and vomiting and very little for its use in x-ray sickness. Rats treated with total body irradiation handle urea nitrogen in the same way whether vitamin B_6 is administered or withheld. However, there is a general belief that roentgen rays exert a damaging effect on many enzyme systems, especially those for which the B complex vitamins serve as coenzymes. If this is true, vitamin B_6 as well as other B complex vitamins might be helpful in reversing damaging effects.

CONCLUSIONS

It is safe to say that vitamin B_6 is a very important nutrient that is essential for human beings; however, deficiency states occur only under unusual circumstances, with manifestations in the skin, mucous membranes, and the central and peripheral nervous systems. Most of the therapeutic claims for vitamin B_6 are still beclouded by uncertainties. Though much more investigation will be necessary before the role of vitamin B_6 as a therapeutic tool will be firmly established, clinicians should be alert to the symptomatology of vitamin B_6 deficiency so that they may recognize deficiency states that may be conditioned by new drugs, new food processing methods, and other changes in our daily life that cannot be predicted at this time.

15. Schreiner, A. W.; Slinger, W. N.; Hawkins, V. R., and Vilter, R. W.: Seborrheic Dermatitis, a Local Metabolic Defect Involving Pyridoxine, J. Lab. & Clin. Med. **40**: 121 (July) 1952.

16. Effersoe, H.: The Effect of Topical Application of Pyridoxine Ointment on the Rate of Sebaceous Secretion in Patients with Seborrheic Dermatitis, Acta dermat.-venereol. **34**: 272, 1954.

17. Wachstein, M., and Gudaitis, A.: Disturbance of Vitamin B_6 Metabolism in Pregnancy, J. Lab. & Clin. Med. **40**: 550 (Oct.) 1952.

18. McGanity, W. J.; McHenry, E. W.; VanWych, H. B., and Watt, G. L.: An Effect of Pyridoxine on Blood Urea in Human Subjects, J. Biol. Chem. **178**: 511 (March) 1949.

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MEDICAL STUDENTS AS SCIENTIFIC DISCOVERERS

Years ago William Osler recorded a pregnant observation in one of his student notebooks. "Experience," he wrote, "is to be measured not by the time served but by the use which a man made of his opportunities." The truth of this comment as it applies to the field of medicine is aptly revealed by Gibson [1] in a recent article on significant scientific discoveries by medical students. Although medical students have played the role of the discoverer for many generations in fields as diverse as chemistry, physics, physiology, anesthesiology, endocrinology, bacteriology, pathology, blood circulation, and neurology, it is apparent that their achievements are not as well known as they might be.

James Blake, who was once called the "Gold Rush Doc," is regarded today as California's first distinguished scientist. While a medical student, at the age of 23, he read a paper before the British Association for the Advancement of Science in which he advanced the theory, based on his own experiments, that the effect of drugs on the body is determined by their chemical structure. He showed that electronegative elements could be arranged in order of their physiological reactions. His grouping of the elements was remarkably similar to that developed 20 years later by Mendeléeff, which is known as the periodic table. Ether was synthesized in 1540 by a student named Valerius Cordus, and a 21-year-old medical student called Humphrey Davy discovered the anesthetic properties of nitrous oxide in Bristol, England. As early as 1800 he wrote: "As nitrous oxide in its extensive operation appears capable of destroying pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place."

The field of physics contains numerous undergraduate contributors. One of them, Willem Einthoven, the son of a doctor, distinguished himself during his first year at the medical school in Utrecht, Netherlands, with a paper on the articulations of the elbow joint and on the mechanism of pronation and supination. In 1884, when he was 25 years old, Einthoven's graduation thesis dealt with stereoscopic vision through color differences, a subject of widespread interest today. Later on, his fame was to grow still further when he introduced the electrocardiograph in medical practice. Fortunately, he lived to see his invention recognized and used during his lifetime.

The investigation that Thomas Young, known as "Phenomenal Young," made on the lens of the eye is a monumental tribute to a 20-year-old medical student who within the following year was to be elected a fellow of the Royal Society of London for his achievement. Young had scarcely begun his anatomy course when he was asked to dissect a recently removed ox eye. The ciliary muscles responded to stimulation, thereby compressing the lens and changing its shape. Young immediately recognized that the alleged lengthening and shortening of the eyeball to accommodate for distance was nothing but a myth.

Claude Bernard, the father of experimental medicine, conducted two investigations during his medical school undergraduate days that were to determine his future career. These were concerned with the secretory nerves to the salivary glands and the digestive function of gastric juice. In this connection, it is interesting to note that the salivary glands were discovered by a Danish medical student, Nicolas Stensen. As a student Bernard also studied the cherry-red color of blood that is present in carbon monoxide poisoning. Walter B. Cannon was a Harvard student whose methods of investigating the digestive tract came to be used the world over. After overhearing a conversation on a Boston streetcar about a new machine that could see right through a fully clothed person, Cannon probed the mysteries of the intestine in cats, geese, dogs, frogs, and human beings, first with buttons, then with bismuth, and later with barium. His work on cats eventually initiated a fresh and fruitful line of investigation—the effect of emotions on body functions.

Medical student discoveries are particularly plentiful in the realm of endocrinology. The insulin-secreting cells of the pancreas were found by Paul Langerhans, a medical student who came from a long line of physicians and pathologists in Jena. In his graduation thesis Langerhans presented findings on the cell types of the pancreas, describing for the first time the islet cells that are now known to produce insulin. Soon after, Ivar Sandstrom, a first year medical student at Uppsala, Sweden, discovered the parathyroid glands, first in the dog and then in man.

Student contributors in the field of the nervous system are legion. A noteworthy example is that of Johannes Purkinje, a young Czech who wrote a medical student thesis on color vision that assured his future. The thesis

1. Gibson, W. C.: Significant Scientific Discoveries by Medical Students, Scient. Month. **81**: 22 (July) 1955.

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attracted the attention of Goethe, the poet-scientist, and, through him, the brothers von Humboldt. As a result, Purkinje was appointed to the chair of physiology at Breslau, Germany. When the local medical academicians protested against the intrusion of a "foreigner" and petitioned Berlin, Germany, for his removal, the Prussian government replied by building for Purkinje's use the first physiological research laboratory in Europe. The undergraduate researches of Charles Sherrington, who has been designated as the "philosopher of the nervous system," are of wide contemporary interest when entire hemispheres of human brain and large tracts of the spinal cord are sectioned. His first paper dealt with the effects of hemisection of the spinal cord and his second one with the effects of removing a single cerebral hemisphere in the dog. These early efforts in the laboratories of Cambridge University were the first steps in a long, distinguished career. The controversy surrounding Sigmund Freud recently has obscured his status as a comparative neuroanatomist. In this connection, what he wrote as a medical student is significant. His figures on the derivation of the T-shaped dorsal root ganglion cells of the spinal cord are used universally, while his work on phylogenetic levels in the development of the nervous system formed the basis for his later theory of the levels of consciousness in man.

The story of the circulation of the blood and lymph is charged with the names of undergraduate investigators. William Harvey was a student investigator at the beginning of the 17th century when he conceived the idea that blood held the secret of circulation. The discovery of the true circulation of lymph in the body is entirely due to three medical students: Pecquet of France, Joyliffe of England, and Rudbeck of Sweden. These students, living hundreds of miles apart, independently described the emptying of the lymphatic system into the great veins.

The twin domains of pathology and bacteriology boast student investigators of the caliber of Paul Ehrlich, Edward Jenner, William G. MacCullum, and René Laennec. As a medical school student, Ehrlich grasped the significance of the selective staining of tissues by means of aniline dyes and wrote his first papers on stains for the blood and stains for lead deposited in tissues. As a result of his unusual ability to picture molecular stereostructure, he predicted many new therapeutic compounds, and, while still a student, developed the basic concepts of his famous side-chain theory. Edward Jenner had scarcely begun his apprenticeship training when he learned that persons afflicted with cowpox were protected from smallpox. William G. MacCullum worked out the life-cycle of malaria in birds while a medical student at Johns Hopkins. Finally, René Laennec, inventor of the stethoscope, wrote a remarkable paper on peritonitis as a 19-year-old student of medicine in Paris.

From the foregoing it is clear that the record of its young students as scientific discoverers constitutes one of the shining chapters in the accomplishments of the medical profession throughout the centuries.

BIRTH AND DEATH CERTIFICATES

The importance of the information furnished by birth and death certificates has become so well recognized that standardization of some of the essential elements has been adopted internationally at the recommendation of the World Health Assembly. Where local problems make other information desirable, modifications or supplementary sheets may be used. The same general plan is followed in the United States, where the Public Health Service has prepared a new form for both certificates, described elsewhere is this issue of THE JOURNAL (page 1184). As with any statistical reporting, the value of the conclusions drawn depends on the completeness and the accuracy of the available data. In order to test the completeness and accuracy of the information reported on a supplemental birth certificate used in Washington, the Bureau of Maternal and Child Health conducted a survey in 1952.[1] From 20 to 44% of the items were found to be incomplete. When the certificates were checked against hospital records, gross discrepancies in the accuracy of the reports were found.

Incomplete records can be returned for completion, but their accuracy must be taken on faith. Physicians, who are rarely in sympathy with paper work, will use their valuable time to fill out these reports more carefully and more willingly if they can be assured that the information requested will really be put to a useful purpose and that supplemental questions will be dropped when this purpose has been achieved. Unfortunately these provisos have not always been observed in the past. Apparently it is easier to set a continuing questionnaire in motion than it is to drop it, but the agencies that use such information can greatly further their aims if they keep the necessity for the information ever before their informants and give them the assurance that their burdens will not be multiplied unduly. The prompt and wide dissemination of reports based on these certificates will give tangible proof of their use and importance.

The new standard forms were designed to keep the certificates up-to-date and to improve accuracy by making some of the questions more specific rather than to introduce innovations. Physicians who fill out these certificates will perform a useful service if they will make sure the information they give is both complete and accurate and if they will use special care in reporting the underlying cause of death.

1. Oppenheimer, E.: Completeness and Accuracy of Medical Information Recorded on Birth Certificates, Am. J. Pub. Health 45:1121-1126 (Sept.) 1955.

ORGANIZATION SECTION

EIGHTH NATIONAL MEDICAL PUBLIC RELATIONS CONFERENCE

Hotel Statler, Boston

Monday, November 28, 1955

The National Medical Public Relations Conference is presented by the American Medical Association as a service to state and county societies. It is open to members of the A. M. A. House of Delegates, to officers and public relations committee chairmen of state and county societies, and to medical society and Woman's Auxiliary representatives working in the field of medical public relations.

PROGRAM

REGISTRATION
9 a.m., Ballroom Assembly Foyer

OPENING SESSION
10:30 a.m., Ballroom Assembly

Chairman: WILLIAM G. H. DOBBS, M.D., Torrington, Conn., Chairman, Public Relations Committee, Connecticut State Medical Society

Your Role for the Day

GEORGE F. LULL, M.D., Chicago, Secretary and General Manager, American Medical Association

Keynote Address: What's Ahead for American Medicine.

DWIGHT H. MURRAY, M.D., Napa, Calif., President-Elect, American Medical Association

Symposium: A Look at '56

DAVID B. ALLMAN, M.D., Atlantic City, N. J., Chairman, A. M. A. Committee on Legislation

JOSEPH D. MCCARTHY, M.D., Omaha, Chairman, A. M. A. Council on Medical Service

F. J. L. BLASINGAME, M.D., Wharton, Texas, A. M. A. Trustee

JAMES C. WORTHY, Chicago, Assistant to the Chairman of the Board, Sears Roebuck and Company

LEO E. BROWN, Chicago, Director, A. M. A. Department of Public Relations

LUNCHEON
12:15 p.m., Ballroom

Where Goes Our Nation?

ERLE COCKE JR., Atlanta, Ga., Vice-President, Delta Airlines

GENERAL SESSION
2 p.m., Ballroom Assembly

Chairman: CONRAD WESSELHOEFT, M.D., Boston, President, Massachusetts Medical Society

Snowballing Social Security

LEONARD E. READ, Irvington-on-Hudson, N. Y., President, Foundation for Economic Education

THOMAS B. CURTIS, Clayton, Mo., Representative, Congress of the United States

Questions and Discussion

The Doctor's Future in America

V. C. ROYSTER, New York, Senior Associate Editor, *Wall Street Journal*

Is Free Enterprise Here to Stay?

WALLACE F. BENNETT, Salt Lake City, U. S. Senator

SUMMING UP: AMERICA '56
4:30 p.m., Ballroom Assembly

EDWARD J. MCCORMICK, M.D., Toledo, Ohio, Past-President, American Medical Association

SPECIAL SCREENING: "BABY TIME"
4:45 p.m., Ballroom Assembly

Screening of new commercial television show produced in cooperation with the American Medical Association

APPEAL FOR CONTRIBUTIONS TO MEDICAL EDUCATION FOUNDATION

A special appeal, the annual American Medical Education Foundation tax mailing, will be sent to all members of the American Medical Association five weeks earlier this year. The appeal will be signed by Dr. Elmer Hess, President of the A. M. A., and will include an AMEF tax folder showing the importance of tax savings by contributing now to the American Medical Education Foundation. During the first nine months of the current campaign, contributions amounted to $540,343.33, compared with $996,198.75 received during the same period last year.

The number of contributors to the Foundation has increased during this period, but the income is $455,855.52 less than it was a year ago. The Foundation has picked up less than $45,000 in individual contributions this year. To maintain last year's record, the Foundation must raise $455,000 during the remaining 10 weeks of the current AMEF campaign. State medical society officers and particularly AMEF state chairmen can give added impetus to the annual tax appeal by contacting county chairmen and enlisting their assistance in personally soliciting donations at the county level.

Five state medical societies have contributed treasury gifts to AMEF during 1955. They include: Massachusetts, $3,000; Tennessee, $1,000; Oregon, $5,000; New Jersey, $25,000; and Virginia, $2,000. Following the Illinois plan (which netted approximately $170,000 for AMEF this year from members of the Illinois State Medical Society), members of the Nevada State Medical Association contributed $3,040 to the Foundation's 1955 campaign. AMEF has also been advised that members of the House of Delegates of the Kansas Medical Society voted treasury gifts in the amount of $2,100 each year for three years, with the moneys earmarked for the Foundation.

At no time has the need been so great for individual financial support of AMEF. The medical profession pledged 2 million dollars annually in 1951 to assist the nation's medical schools, and AMEF income exceeded 1 million dollars in 1953 and 1954. Unless increased individual support is forthcoming during the remaining 10 weeks of the 1955 campaign, the Foundation's total income will be the lowest in its history. Take advantage of the special tax appeal and contribute to AMEF now! With the support of every member of the medical pro-

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fession, the Foundation can achieve its annual 2 million dollar goal and maintain high medical teaching standards without federal subsidies.

LAHEY AWARD TO HERBERT HOOVER

Former President Herbert Hoover was presented the Frank H. Lahey Memorial award Oct. 19 in his apartment at the Waldorf-Astoria Towers, New York. The presentation was made by S. Sloan Colt, New York, president of the National Fund for Medical Education, of which Mr. Hoover is honorary chairman. Present were Dr. Elmer Hess, of Erie, Pa., President of the American Medical Association, and Dr. Joseph C. Hinsey, director of New York Hospital–Cornell Medical Center, representing the Association of American Medical Colleges. The two medical associations and the National Fund for Medical Education jointly sponsor the Lahey award for outstanding leadership in medical education.

Left to right: Joseph C. Hinsey, S. Sloan Colt, Mr. Hoover, and Elmer Hess.

Mr. Colt told the former President: "You saw our great universities facing financial disaster through the cost of maintaining medical schools that were fast becoming a serious drain on their parent institutions. Your vision comprehended the continuing role of research in the advancement of medical skills and the alleviation of disease. And you recognized the debt owed by industry and the business community to the benefits of medicine, a debt that must be acknowledged in their support of the medical schools."

In accepting the award, Mr. Hoover declared that the responsibility for finding funds for the medical schools "does not lie upon our medical men but upon laymen and industry. . . . The nation is indebted for this great effort to set medical education and medical research on the road to solvency for upon it rests the health and security of our people."

The National Fund for Medical Education was formed in 1949 under the leadership of former President Hoover; President Eisenhower, at that time president of Columbia University; Dr. James B. Conant; and other educators and university presidents. President Eisenhower was the first recipient of the Lahey award in a ceremony at the White House last November. In the brief period since organization of the fund, nearly 9 million dollars has been raised from industry, the medical profession, foundations, and individuals.

FEDERAL MEDICAL LEGISLATION

First Session, 84th Congress

The 84th Congress convened Jan. 3, 1955, and adjourned sine die Aug. 2, 1955. During this period 11,914 legislative measures were introduced in the Senate and House. All of these were screened for possible medical significance, and 404 were summarized and reported by the Washington Office of the A. M. A., roughly, 3.4% of all the measures introduced. This is only 3 less than were reported in both sessions of the 83rd Congress and is 156 more than were reported in both sessions of the 82nd Congress. The chief legislative measures are briefly summarized below.

Numerically, the most common measures of interest to the medical profession as such dealt with social security. Of 58 such bills, none became public law. A series of amendments to the Social Security Act were proposed in H. R. 7225, which was passed by the House without hearings and without the opportunity to make amendments on the floor. One day's open hearing to receive the administration's viewpoint on this measure was held in the Senate, but no further hearings were held and no further action was taken on the bill. This would include, among other provisions, the lowering of the age at which disabled covered employees could receive cash retirement benefits from 65 to 50. Veterans' legislation was proposed in 46 different measures, none of which became public law.

Salk vaccine was the subject of 33 measures and much argument and lengthy hearings on how far the government should go in the control and distribution of the vaccine. The resulting measure was Public Law 377, which provided 30 million dollars in grants to be used by Feb. 15, 1956, to help the states finance state immunization programs. Tax deductions were proposed in 29 measures, but none became public law, although the Jenkins-Keogh proposal, H. R. 9 and 10, was acted upon favorably by the House Finance Committee but not reported to the House. This measure would allow tax postponement for limited amounts placed in selected retirement funds.

Military Medicine and Defense

There were 26 proposals dealing with military medicine and defense matters. One of these, S. 2587, would give military status to the commissioned officers of the Public Health Service during periods of national emergency as well as during war. The bill was reported to the Senate floor without hearings and passed, but no hearings were held in the House and the measure was not voted out of Committee there. The "Doctor-Draft" act was extended for two years as a part of a measure extending the basic Selective Service Act and certain benefits for the dependents of the men in uniform. Included

Prepared by the Washington Office of the American Medical Association.

was the $100-per-month equalization pay for physicians, dentists, and veterinarians. The "Doctor-Draft" act was modified to lower the age limit for call from 51 to 46 years. A new provision would provide that any physician rejected on application for a commission solely for physical reasons would no longer be liable for induction on reaching age 35. The Public Law is 118. There was no chance to have a clear-cut vote on just the doctor draft. At the present time, however, new legislation is prepared to make the military medicine more attractive as a career, thus eliminating the need for the extension of the doctor draft.

Reserve commissions were authorized for male nurses in the armed services by Public Law 294. A measure to commission osteopaths in the Medical Corps of the armed services passed the House but was assigned to a special committee in the Senate; no hearings were held and no further action taken. Measures to provide medical care for the dependents of the uniformed services were introduced but no hearings held. Committee work is continuing on this subject.

Agency for Handicapped, Mental Health, and Drug Addiction

A proposal to establish an independent agency for the handicapped, placed for housekeeping purposes in the Department of Labor, was proposed in 23 measures. Hearings were not held and no action taken on any of the bills. Mental health was the subject of 18 measures introduced in the first session. From these measures, Public Law 182 was passed, which authorized the appropriation of $1,250,000 over a three-year period to make a survey of mental health problems and existing programs in this field. This study would be conducted by a nongovernment group or groups, and $250,000 was appropriated for the first year. Hearings were held in the House and a bill favorably reported that would provide for construction of hospital and other facilities for a mental health program for the mentally ill of Alaska, but the measure was not voted upon. Hearings were held on the administration's proposal for direct grants to states on the need, population, per-capita-income formula for mental health programs, but no action was taken.

Drugs and drug addiction were the subjects of 17 proposals. Authority was given to the Commissioner of Narcotics to subpoena narcotics records by Public Law 362. The Senate passed a measure to authorize the Senate Judiciary Committee to study the narcotics problem in the United States and hearings are now being held.

Miscellaneous Bills

A series of 16 bills was devoted to medical education. Hearings were held in both the House and Senate on a measure to provide construction grants for medical schools, but no further action was taken. Hearings were held on a military medical scholarships bill in the House, but the bill was not reported. Water and air pollution was the subject of 16 measures, of which one, S. 928, became Public Law 159. This authorized a 25 million dollar appropriation over a five-year period for grants to states, local governments, private groups, and individuals for research, training, and demonstration projects in air pollution abatement. A measure to allow the shipment of live scorpions in U. S. mail became Public Law 108.

A number of other measures received committee attention, and some passed one House but not the other. Those passing one House included a proposal to give grants to construct laboratory research facilities; another would extend the Water Pollution Control Act until 1960 and authorize an appropriation of 2 million dollars a year in grants for pollution prevention. Those upon which hearings were held but no further action taken included a proposal to provide teaching grants and scholarships for practical and professional nursing training. Another measure that would amend the Biologics Control Act to give the Secretary of the Department of Health, Education, and Welfare authority to control both distribution and use of certain biologicals got no further than the committee hearings. A subcommittee of the Senate Judiciary Committee held hearings on the Bricker amendment, which would limit the treaty-making powers of the President. All measures not acted upon are still before the committees and can be acted upon until the close of the 84th Congress, which starts sessions again in January.

NEW PUBLICATIONS

To All My Patients, a leaflet briefly explaining the role of the various members of the medical team and discussing health insurance, medical care service, fees, and other aspects of medical practice. Designed for distribution by physicians to their patients, perhaps as an enclosure with their monthly statements or in their reception rooms. Copies may be had by addressing the Public Relations Department at A. M. A. headquarters.

Report on Medical Care for the Indigent, a booklet giving the findings of staff members who visited 11 communities and seven states for the Committee on Indigent Care to learn the characteristics of their organized indigent medical programs. Most of this material is a reprint from various recent issues of THE JOURNAL of articles originally prepared by the Council on Medical Service.

Roster of Executives of State and County Medical Societies. This pamphlet, prepared by the Council on Medical Service, is a revision up to September, 1955, of previous lists of state and county medical society executives along with their addresses and telephone numbers; it contains also a roster of state and county society journal editors.

What's Up with Our Medical Schools? prepared by the A. M. A., highlights the progress being made in medical education in the United States.

Do You Make Par as a Patient? reprint from *Family Weekly* magazine, asks patients pertinent questions designed to find out if they are good patients.

Free Health Care for Everyone? from the United States Chamber of Commerce, discusses the economics of medical care in the nation.

The last three publications are being made available to state and county medical societies for distribution to the public.

MEDICAL NEWS

CALIFORNIA

Fund for Cancer Research.—A $100,000 trust fund for cancer research at the medical center on the Los Angeles campus of the University of California has been established by James and Lorena Greims of Encino. The fund will be used for certain surgical problems associated with cancer under the direction of Dr. George A. Stevens, clinical professor of surgery.

Dr. Holman Honored.—The August number of the *Stanford Medical Bulletin* was issued as a "Festschrift" for Dr. Emile F. Holman, San Francisco, who retired Sept. 1 as head of the department of surgery at the Stanford University School of Medicine after 30 years of service on the faculty. The special issue contains 25 articles contributed by his colleagues and former students. Dr. Arthur L. Bloomfield, emeritus professor of medicine, in the introduction to the Festschrift said, "Dr. Holman has always possessed in high degree that fundamental curiosity which is the essential prerequisite for true research. In all he has no less than 163 titles to his credit."

University News.—Plans to build a $1,500,000 basic science building for the University of Southern California School of Medicine across from the Los Angeles County Hospital were announced recently. The building will consolidate all medical instruction of the university on one campus. On the lower floors will be facilities for undergraduate laboratories in biochemistry, physiology, pharmacology, pathology, microbiology, and anatomy. On the upper floors will be faculty offices and research laboratories. There will also be a serles of larger laboratories for advanced specialized research. When other funds become available, a second unit of the basic science building will be built. Also planned are a medical library, an auditorium, a student cafeteria, and administrative offices. When the entire project is completed, the medical center will occupy a 10 acre area and will cost about 5 million dollars.

DISTRICT OF COLUMBIA

Hospital News.—At the annual outing of the Providence Hospital Alumni Association it was announced that the one million dollar goal of the New Providence Hospital Building Fund had been exceeded. Providence doctors raised $147,874 among themselves, exceeding their quota by $35,000. The eight million dollar hospital now under construction in Washington, D. C., is expected to be completed by December.

ILLINOIS

Downward Trend of Disease.—According to the State Department of Public Health, case reports for all but 4 of some 21 notifiable diseases were lower in the first three quarters of 1955 than in the corresponding period of 1954. Among the diseases showing significant declines this year are: infectious hepatitis, with a reduction in case reports of about 50%; poliomyelitis, 30%; syphilis, 11%; and pneumonia and influenza combined, 10%. Case reports of measles dropped from 32,026 in the first 9 months of 1954 to 12,087 this year, whereas scarlet fever declined from a total of 3,086 cases to 2,334. The four diseases responsible for higher morbidity this year than in the first three quarters of 1954 are chickenpox, with an increase in case reports of about 60%; tuberculosis, 22%; mumps, 18%; and gonorrhea, 6%.

Chicago

Dr. Braceland to Lecture.—The inaugural address in neuropsychiatry of the Leo A. Kaplan Memorial Lectureship of the Phi Delta Epsilon Foundation will be given at the Drake Hotel on the evening of Nov. 29 by Dr. Francis J. Braceland, psychiatrist-in-chief, Institute of Living, Hartford, Conn. Dr. Braceland is president-elect of the American Psychiatric Association.

Appoint Associate Professor of Ophthalmology.—Dr. Bertha A. Klien has been appointed associate professor of ophthalmology in the department of surgery, University of Chicago School of Medicine. Dr. Klien is a winner of the A. M. A. gold medal for a scientific exhibit on Diseases of the Fundus Oculi, which was awarded at the 1948 meeting of the A. M. A. in Chicago, and of the silver medal of the Illinois State Medical Society.

Course on Arrhythmias.—An advanced course on interpretation of complex arrhythmias (intended only for experienced electrocardiographers) will be given at Michael Reese Hospital by Drs. Louis N. Katz, Richard Langendorf, and Alfred Pick. The class will meet daily from 9 a. m. to 5 p. m., Dec. 5-9. Information may be obtained from Secretary, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago 16.

Grants and Fellowships in Cardiology.—The Chicago Heart Association offers grants-in-aid for research in cardiovascular diseases and related fields, ranging up to a maximum of $10,000. Grants, made for a fiscal year that runs from July 1 to June 30 inclusive, may be renewed on application and annual review. Completed application is due Dec. 1, to be effective the following July. For information write to: Chicago Heart Association, 69 W. Washington St., Chicago 2, Attention: Program Coordinator.

Society News.—Newly elected officers of the Chicago Urological Society include: Dr. Joseph H. Kiefer, president; Dr. Knowlton E. Barber, vice-president; and Dr. Don E. Murray, secretary-treasurer.——Newly elected officers of the Chicago Society of Allergy include: Dr. Simon S. Rubin, Gary, Ind., president; Dr. Helen C. Hayden, president-elect; and Dr. Norman J. Ehrlich, secretary-treasurer.——The Chicago Society of Internal Medicine recently elected Dr. Arthur R. Colwell, president; Dr. Fred E. Ball, vice-president; and Dr. Franklin A. Kyser, Evanston, secretary-treasurer.——Newly elected officers of the Chicago Gynecological Society include: Dr. Magnus P. Urnes, president; Dr. Ronald R. Greene, president-elect; Dr. Solomon J. Benensohn, vice-president; Dr. Robert A. Beebe, treasurer; and Dr. Clyde J. Geiger, secretary.

KANSAS

Training in Administrative Psychiatry.—An experimental training program in psychiatric hospital administration has been initiated at the Menninger Foundation, Topeka, with cooperation from the Winter Veterans Administration Hospital and Topeka State Hospital. First trainees in the project are Dr. Robert Allen Haines, on leave as superintendent of Apple Creek (Ohio) State Hospital, and Dr. George Zubowicz, formerly director of allied clinical services at Topeka State Hospital. The program is the first to provide a one-year formal training period required by the American Psychiatric Association, which in 1953 issued standards for examining and certifying medical hospital administrators. Dr. Robert C. Anderson, manager of Winter Veterans Administration Hospital, is director of the program. Physicians wishing information about the program may write to John R. Malban, assistant director of the program, at the Menninger Foundation, Topeka.

KENTUCKY

"Oscar Allen Day."—The citizens of Beaver Dam and its surrounding countryside recently honored Dr. Oscar Allen for his 50 years of service to the community. Dr. Arthur T. Hurst, Louisville, vice-president, Kentucky State Medical Association, represented Dr. Clyde C. Sparks, Ashland, president, Kentucky State Medical Association, along with Dr. Walter L. O'Nan, Henderson, councilor for the second district, in which Dr. Allen

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

lives, and Dr. J. Gant Gaither, Hopkinsville, the association's president-elect. Music played during the program was by an orchestra made up entirely of Dr. Allen's grandchildren. After the ceremony a reception was held at the school.

MAINE

Course in Infectious Diseases.—A refresher course in infectious diseases is offered at the Central Maine General Hospital, Lewiston, by Dr. Louis Weinstein, associate professor of medicine, Boston University School of Medicine. Dr. Weinstein's lecture Nov. 23 (1-4 p. m.) will concern infections of the cardiovascular system, including bacteremia, septicemia, endocarditis, and thrombophlebitis, and recent concepts in the treatment of rheumatic fever. On Dec. 1 he will consider infections of the nervous system.

MASSACHUSETTS

Hospital Centennial.—Massachusetts Memorial Hospitals, Boston, will celebrate its centennial, Nov. 21, with an all-day session about "Health for the American People." Massachusetts Memorial Hospitals, which served 26,000 patients last year, is a group comprising the Evans, Collamore, Robinson, and Talbot memorial hospitals on Harrison Avenue, the Haynes Memorial Hospital on Allston Street, and the Medical Associates on Commonwealth Avenue in Boston. It is closely integrated with the Boston University Medical School. Dr. Chester S. Keefer is physician-in-chief of the hospital group and director of the medical school. Dr. Philip D. Bonnet is administrator of the hospitals. On Sunday, the day preceding the official centennial celebration, the public is invited to an open house at the main hospital on Harrison Avenue. All other sessions will be at the Hotel Statler. Monday will be devoted to panels on organization of health services, paying for health services, and community action for health. Physicians participating will include: Dr. Keefer; Drs. Dean A. Clark, general director, and Robert W. Wilkins, associate physician-in-chief of the hospitals; and Drs. Edwin F. Daily, New York, Donald M. Clark, Andover, Mass., George Crile Jr., Cleveland, and Leonard A. Scheele, Washington, D. C. The centennial banquet address, 7 p. m., will be delivered by Dr. Howard A. Rusk, professor of physical medicine and rehabilitation, New York University College of Medicine, New York City.

MICHIGAN

Dr. Buxton Goes to Baltimore.—Dr. Robert William Buxton, formerly associate professor of surgery, University of Michigan Medical School, Ann Arbor, has been appointed chairman, department of surgery, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore. Dr. Buxton was formerly affiliated with the Strong Memorial Hospital and Genesee Hospital in Rochester, N. Y.

NEBRASKA

Dr. Potthoff Named Director of Preventive Medicine.—Dr. Carl J. Potthoff has been appointed director of the department of preventive medicine at the University of Nebraska College of Medicine, Omaha. Previously Dr. Potthoff had been associate national medical director of the American Red Cross and had divided his time between the department of preventive medicine and the Omaha-Douglas County Health Department, where he served as assistant commissioner of health.

NEW YORK

Dr. Babbott Honored.—Dr. Frank L. Babbott, former president of the Long Island College of Medicine, Brooklyn (now the State University of New York College of Medicine at New York City), was awarded the honorary degree of doctor of laws during the centennial celebration of the Polytechnic Institute of Brooklyn, of which he has been a member for 29 years.

Lucien Howe Medal to Dr. Bedell.—At a recent meeting of the American Ophthalmological Society, Dr. Arthur J. Bedell, Albany, was awarded the Lucien Howe medal in recognition of his distinguished service in ophthalmology. Dr. Bedell, professor emeritus of ophthalmology at Albany Medical College since 1941, is attending ophthalmologist at St. Peter's Hospital, the Child's Hospital, the Old Ladies Home, and the Albany Home for Children. He was the A. M. A. delegate to the British Medical Association in 1936, winner of the A. M. A. silver medal for a scientific exhibit in 1928. The Section on Ophthalmology has bestowed on him its Prize Award in Ophthalmology and the Herman Knapp gold medal. The Medical Society of the State of New York awarded him the Lucien Howe prize for research in ophthalmology in 1922, 1924, 1927, 1936, and 1938, and the University of Buffalo the Howe Ophthalmological prize this year (THE JOURNAL, July 9, 1955, page 858).

School for Retarded Children.—Governor Averell Harriman has announced that the department of mental hygiene will construct a school for retarded children in West Seneca in Erie County. The school, expected to cost more than 30 million dollars, is the first of four institutions planned under the department's building program, for which voters approved a 350 million dollar bond issue in 1954. Designed for 2,400 patients, it will be provided with service facilities for future expansion, if required, to 3,000. The school will be constructed on a modified cottage plan in which all buildings will contain dining rooms, making it unnecessary for the children to leave their home buildings for meals. The kitchens will be centralized. The school will also include a hospital to care for the acutely ill, classrooms and vocational training facilities for the educable, a training center for the more severely retarded, facilities for a rehabilitation service for the physically handicapped, and a special building for very young children. It is also planned to provide small units for a special psychiatric program for children who show transient emotional disturbances. The school will serve the counties of Erie, Niagara, Orleans, Genesee, Wyoming, Allegany, Cattaraugus, and Chautauqua, with about 75% of the prospective patients coming from Erie and Niagara counties.

New York City

Doctors' Orchestral Society.—The Doctors' Orchestral Society of New York held its first rehearsal Sept. 29, at Public School 33, Ninth Avenue and 26th Street. Rehearsals are held every Thursday at 8:15 p. m. Several concerts are planned for this season under the direction of the new conductor, Mr. Maxim Waldo. Dr. Alfred E. Mamelok (115 E. 61st St., New York 21) is president of the group. All musician members of the medical profession or allied healing arts are invited to join the orchestra.

Dr. Louis Bauer Honored.—Dr. Louis H. Bauer, secretary-general, World Medical Association, and past-president, American Medical Association, recently was awarded the degree of doctor of science, honoris causa, by the University of Sydney, Australia. Dr. Bauer presented the Sir Henry Simpson Newland Oration at the ninth Australasian Medical Congress in Sydney and the Joseph Bancroft Oration before the Queensland Branch of the Australian Medical Association in Brisbane. Before returning to the United States, he visited various branches of the British and Australian medical associations and also the headquarters of the Philippine Medical Association in Manila.

Dr. Cahill Retires as Director.—Dr. George Francis Cahill is retiring as director of the urologic service and as professor and executive officer at Columbia University but will continue to serve as consultant to the hospital and professor emeritus. Dr. Cahill, one of those who helped build up the J. Bentley Squier Urological Clinic, plans to write a history of the clinic, raise funds for its expansion, and, with other staff urologists and physicians, prepare a textbook on the adrenals. Among his major contributions are his classification of tumors of the adrenals and, with Dr. Marcel Goldenberg, the initiation of a test for pheochromocytoma. Dr. Cahill has been president of the American Urological Association and of the American Board of Urology, is consultant to numerous hospitals, and, from 1946 to 1949, was president of the Presbyterian Hospital's medical board.

Personal.—Dr. Joseph E. Rall has been selected as head of the clinical endocrinology program at the National Institute of Arthritis and Metabolic Diseases, Bethesda, Md.——Dr. Paul S. Seager, who has been affiliated with the New York University

Postgraduate Medical School since 1935, has been promoted to professor of clinical otorhinolaryngology.——Charles Glen King, Ph.D., scientific director of the Nutrition Foundation, New York, has been appointed a member of the National Advisory Arthritis and Metabolic Diseases Council.——Dr. Gregory Zilboorg, clinical professor of psychiatry, State University of New York College of Medicine at New York City, addressed the Long Island Psychiatric Society at the Veterans Administration Hospital, Northport, L. I., on "Growing Conflicts Between Clinical and Theoretical Psychiatry."——Dr. Frederick S. Reiss, associate clinical professor of dermatology, New York University Post-Graduate Medical School, recently attended the International Medical Conference in Verona, Italy, where he participated in the symposium on stress and lectured on "Stress and Psoriasis."——Dr. Franz J. Kallmann, professor of psychiatry, Columbia University College of Physicians and Surgeons, recently addressed the members of the hospital staff of the Veterans Administration Hospital at Northport, L. I., on "Genetic Aspects of Preadolescent and Adult Forms of Schizophrenia."

NORTH CAROLINA

Cruise Conference for Practitioners.—The North Carolina Academy of General Practice will present a postgraduate course, including 25 hours of formal teaching, aboard the M. S. Stockholm, a transatlantic liner that will sail from Wilmington, Nov. 23. During the 12-day cruise, stops will be made at Port-au-Prince in Haiti; Cartagena, on the coast of the Republic of Colombia; the San Blas Islands; Cristobal in the Canal Zone; and Kingston, Jamaica. The cruise, operated by the Allen Travel Service, Inc., 550 Fifth Ave., New York 36, will be sponsored by the Duke University School of Medicine, Durham. The faculty will include: Drs. William McNeal Nicholson, Wilburt Cornell Davison, F. Bayard Carter, Barnes Woodhall, and J. Lamar Callaway.

PENNSYLVANIA

Personal.—Dr. Robert A. Moore, vice chancellor, schools of the health professions, University of Pittsburgh, has been appointed to the National Advisory Cancer Council.——Dr. Henry R. O'Brien joined the staff of the Pennsylvania State Department of Health, Harrisburg, as director of professional training, Aug. 1, following his retirement from the regular corps of the U. S. Public Health Service.

Cardiovascular Research.—The Pennsylvania Hospital, Philadelphia, announces an agreement with the Edna G. Kynett Memorial Foundation to augment the research and teaching facilities in cardiovascular diseases at the hospital. New quarters are being prepared on the fourth floor of the Out-Patient Building. The new, air-conditioned quarters will include space for the present heart station as well as ballistocardiography, cardiac catheterization, and fluoroscopy. The facilities will also include a waiting room for patients, doctors' offices, laboratories, and a library. The foundation and the hospital will share the expense of preparing the new quarters, which necessitates moving the dental and genitourinary clinics and the physical therapy department. The foundation will contribute funds for research equipment and technicians' salaries. The residents and research fellows of the cardiovascular department and the division of medicine of the Pennsylvania Hospital will participate in the new teaching and research programs. Dr. Stephen B. Langfeld will be the director of research for the foundation. Dr. Joseph B. Vander Veer, head, cardiovascular department, Pennsylvania Hospital, will coordinate the services. The new facilities are expected to be ready for occupancy Jan. 1, 1956.

Philadelphia

Semicentennial Celebration.—The section on medical history of the College of Physicians of Philadelphia will observe the semicentennial anniversary year of its founding Nov. 22. After a dinner at the hall of the college (7043 Elmwood Ave.), there will be an address, "Expanding the Use of the Library's Historical Collections," by Walton B. McDaniel II, Ph.D., curator of the Library Historical Collections at the College of Physicians of Philadelphia.

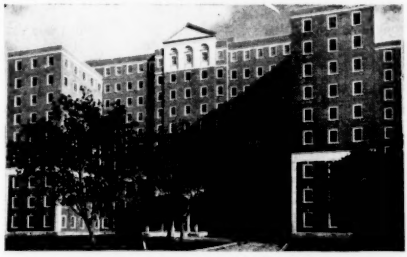
Ophthalmology Chairman Appointed.—Dr. Irving H. Leopold has been appointed chairman of the department of ophthalmology in the University of Pennsylvania Graduate School of Medicine, where he has been a faculty member since 1946. He succeeds Dr. Edmund B. Spaeth, department head for the last 12 years, who is relinquishing the chairmanship but will continue to teach and practice. Dr. Leopold also is director of the research department of Wills Eye Hospital and an attending physician at the hospital. He is in charge of the home study course in physiology of the American Academy of Ophthalmology and Otolaryngology and has served as an associate editor of the *A. M. A. Archives of Ophthalmology*, a consultant to the medical research division of the Army Chemical Warfare Service, and a consultant to the U. S. Public Health Service's study section for neurological diseases and blindness.

SOUTH CAROLINA

Society News.—Newly elected officers of the South Carolina Radiological Society include: Dr. George W. Smith, Columbia, president; Dr. Willis S. Hood, Greenville, vice-president; and Dr. Samuel W. Lippincott, Charleston, secretary-treasurer.

Personal.—Dr. Robert C. Rendtorff, formerly of Columbia, has joined the staff of the University of Tennessee College of Medicine, Memphis, as assistant professor of preventive medicine. He previously was connected with the virology laboratory of the University of Michigan, Ann Arbor.

Medical College Hospital.—The 11 million dollar Medical College Hospital, which adjoins the Medical College of South Carolina in Charleston, was opened for public inspection on Aug. 10. The hospital, which occupies the entire block bound



Medical College Hospital in Charleston.

by Ashley, Mill, Lucas, and Doughty streets, was built with state and Hill-Burton funds on property provided by the county of Charleston. The first hospital built by the college was erected in 1840 at the west end of Broad Street "for the purpose of furnishing instruction at the bedside of the sick, for Medical Students in the annual Classes." The new 10-story hospital has about three miles of corridors. Two emergency generators turn on automatically in two seconds when power is cut off and within six seconds build up power to carry the entire electrical load. Oxygen, piped throughout the building, is available almost everywhere for instant use. According to Dr. Kenneth M. Lynch, president of the Medical College of South Carolina, five state administrations have had a part in planning, building, and opening the new hospital. The dedication ceremonies (May 10), at which Dr. Lynch presided, were opened by Dr. Thomas A. Pitts, chairman, board of trustees. Messages were presented by Dr. Thomas R. Gaines, Anderson, president, South Carolina Medical Association; Dr. John W. Cronin, medical director, chief, Division of Hospital Facilities, U. S. Public Health Service, Washington, D. C.; and Dr. Herman G. Weiskotten, Skaneateles, N. Y., chairman, A. M. A. Council on Medical Education and Hospitals. The dedicatory address was delivered by George Bell Timmerman Jr., governor of South Carolina.

TENNESSEE

Society News.—The Tennessee Radiological Society recently elected Dr. John M. Wilson, Memphis, president; Dr. Ben R. Mayes, Nashville, vice-president; and Dr. George K. Henshall, Chattanooga, secretary-treasurer.

Dr. Freeman Day.—The community of Granville recently honored Dr. Luther M. Freeman when the three churches united in Sunday morning service. In the after-dinner parade Dr. Freeman rode in a 1916 Model-T Ford such as he used in his practice for many years. On a plaque presented to him was inscribed: "To our beloved country doctor, L. M. Freeman, for his untiring years of faithful service in and around the community of Granville, Tennessee, on this day, July 24th, 1955, which marks fifty golden years of medical attention to us."

Personal.—Dr. Douglas H. Sprunt, Memphis, has been appointed to the cancer control committee of the National Cancer Institute of the U. S. Public Health Service.——Dr. Louis F. Rittelmeyer Jr., assistant director, general practice department, University of Tennessee College of Medicine, Memphis, has been named assistant professor of preventive medicine in charge of general practice at the University of Mississippi School of Medicine, Jackson. Dr. Rittelmeyer, formerly of Mobile, Ala., has been affiliated with Mercy Hospital in Chicago and City Hospital in Mobile.——Dr. Ralph M. Kniseley, scientist with Oak Ridge Institute of Nuclear Studies, resigned Aug. 26 to accept a post with the Eden Hospital, Castro Valley, Calif. Before coming to Oak Ridge, he held positions with the Mayo Foundation, Rochester, Minn., and the Lovelace Clinic in Albuquerque, N. Mex.

TEXAS

Hospital News.—The 10 million dollar Parkland Memorial Hospital at 5201 Hines, Dallas, was recently dedicated some 15 blocks from the previous location. The 588-bed hospital, which will still serve as the teaching hospital for Southwestern Medical School of the University of Texas, will provide about twice the space of the old hospital, with an estimated 30% increase in personnel.

Medical Research Foundation.—The Medical Research Foundation of Texas, Inc., announces the selection of the following board of directors: Drs. J. Layton Cochran, president, Texas Medical Association, San Antonio; Francis J. L. Blasingame, Wharton; Hyman W. Paley, Edgar J. Poth, John E. Johnson Jr., Carl A. Nau, and Titus H. Harris, all of Galveston. The purpose of the foundation is to provide funds to medical and dental schools throughout Texas for fellowships and consultantships in research fields in medicine and for the purchase of equipment that cannot be purchased with funds available from other sources. The executive offices are located at University Station in Galveston.

VERMONT

State Medical Election.—Newly elected officers of the Vermont State Medical Society include: Dr. W. Douglas Lindsay, Montpelier, president; Dr. Philip H. Wheeler, Brattleboro, president-elect; Dr. James P. Hammond, Bennington, vice-president; Dr. Robert L. Richards, Grafton, secretary; and Dr. David Marvin, Essex Junction, treasurer.

VIRGINIA

Pathologists Meet in Richmond.—A joint meeting of the Virginia Society for Pathology and the Middle Eastern Region, College of American Pathologists, will be held at the John Marshall Hotel, Richmond, Nov. 26. The program of the morning session, presided over by Dr. Edward D. Levy, Norfolk, follows:

Cell Virus Relationships, Igor Tamm, New York.
Tissue Reaction to Viruses, John P. Wyatt, St. Louis.
Laboratory Diagnosis of Virus Disease, Morris Schaeffer, Montgomery, Ala.

Dr. Arnold F. Strauss, Norfolk, will preside at the afternoon session, during which a slide seminar on virus disease with inclusions will be presented by Drs. Henry Pinkerton and John P. Wyatt, professors of pathology, St. Louis University School of Medicine. Wives of guests are cordially invited to the social hour and dinner (dress informal) at 6 p. m.

Licensure Denied.—The board of medical examiners reports that licensure was denied Dr. Leslie Upton, both by endorsement and examination, on April 7, 1953. Dr. Upton first applied to the board in May, 1951, submitting credentials including an M.D. degree from Middlesex University School of Medicine, Waltham, Mass. According to his credentials he was given credit at Middlesex University for one year of studies completed at the Royal Elizabeth University School of Medicine of Hungary. His application was refused on the basis of the board's requirement that the school of graduation must be registered with the State Board of Education of Virginia as maintaining at the time of such study a standard satisfactory to the board of education based on the grading of the American Medical Association. The latter body has never approved the school. Dr. Upton filed a petition in the circuit court of Fairfax County, Virginia, requesting the court to require the board of medical examiners to show cause why he should not be granted a license under certain reciprocal arrangements in effect between Virginia and the states of Massachusetts and New York, respectively, and, if this relief should not be granted, to require the board to show cause why he should not be admitted to the examination given by the board. In its answer the board denied the existence of any full reciprocal relationship between Virginia and these states and alleged that, as the petitioner's school of graduation did not measure up to statutory requirements for admission to the Virginia examinations, it had no discretionary power to accept his application. The case was fully heard by the court on April 7, 1953; the findings of the board were confirmed; and the petition of Dr. Upton was dismissed. The statute provided that the judgment of the court on the issue was final and not subject to appeal.

WEST VIRGINIA

Memorial Fountain.—A fountain and pool on the grounds of Davis Memorial Hospital, Elkins, were dedicated Sept. 25 to the memory of Dr. Arthur Parker Butt Jr., who died in 1953. The eulogy was delivered by Dr. Charles L. Leonard, Elkins, who was long associated with Dr. Butt in his practice at the hospital. The memorial was donated by friends and associates of the late Dr. Butt.

Personal.—Dr. Herbert M. Beddow, Charleston, was elected president of the West Virginia chapter of the Medical College of Virginia Alumni Association at the annual meeting at White Sulphur Springs, Aug. 20.——Dr. David C. Prickett, recently released from the U. S. Public Health Service after serving as medical officer in charge of a field health center at the Navajo Reservation in New Mexico, has located at Fairmont, where he will engage in general practice.——Dr. Lawrence F. Boland, who has practiced medicine and surgery in Mingo County for 30 years, has accepted appointment as medical director of the Kentucky Training Home, an institution for the care of mentally retarded children and adults, at Frankfort. Formerly located at Sone, Ky., Dr. Stone moved to Williamson in 1921, where he has since practiced industrial surgery.

Grants for Rural Health Centers.—William T. Sanger, Ph.D., Richmond, past-president of the Medical College of Virginia, Richmond, now consultant to the Laird Foundation of Montgomery, announces substantial grants to the foundation by the Avalon and Old Dominion foundations, established by the family of the late Andrew W. Mellon, former secretary of the treasury, which will result in the development of a group of rural health centers in southern West Virginia. The first medical center will be built at Summersville. Over-all plans include expansion of present facilities at Laird Memorial Hospital in Montgomery, a division of Laird Foundation. The rural health centers or clinics will be constructed, equipped, staffed, and operated under the sponsorship of the Laird Foundation, a nonprofit corporation established several years ago "for the relief of suffering, the encouragement of medical education, and the promotion of research." They will include space for offices of physicians, examining rooms, laboratories, and bed space for obstetrical and emergency patients.

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GENERAL

Iodine Research Award.—The Chilean Iodine Educational Bureau award for 1955 was presented to Domenick Papa, Ph.D., New Jersey chemist, at the annual meeting of the American Pharmaceutical Association in Miami, Fla. Dr. Papa was nominated for the award in acknowledgment of his research in the chemistry of iodine and its compounds as applied in pharmacy and medicine. He has been engaged for the past 14 years in research on iodine compounds and synthetic medicinal agents.

Selected Readings on Rehabilitation.—The Illinois Public Aid Commission, Springfield and Chicago, has assembled in a paperbound book 159 pages of previously published articles by physicians, social workers, and lay writers on various phases of the broad subject of rehabilitation. The object was to select material that would be balanced, suggestive, and helpful toward an understanding of the nature, meaning, and objectives of rehabilitation and to attempt to present the best current thinking in this field.

Relationship of Work to Heart Attacks.—The American Heart Association will support and supervise a study on the relationship between work and exercise and heart disease and heart attacks directed by Dr. Sidney R. Weinberg, assistant medical examiner of New York City. The project will be under the jurisdiction of a joint committee on strain and trauma. A project is also being organized that will have as its purpose the critical analysis of legal decisions concerning cardiovascular cases in relation to workmen's compensation.

Van Meter Prize Award.—The American Goiter Association again offers the Van Meter prize award of $300 and two honorable mentions for the best essays submitted on original work on thyroid gland problems. The awards will be made at the annual meeting of the association at the Drake Hotel, Chicago, May 3-5, 1956. The competing essays may cover either clinical or research investigations, should not exceed 3,000 words, and must be in English. Duplicate typewritten copies, double-spaced, should be sent to the secretary, Dr. John C. McClintock, 149½ Washington Ave., Albany, N. Y., not later than Jan. 1, 1956.

Program in Human Engineering.—The Mellon Institute of Industrial Research, University of Pittsburgh, announces the free availability of a new publication, "Proposed Program in Ergonomics—Human Engineering" by Theodore F. Hatch, S.M., professor of industrial health engineering, Graduate School of Public Health, University of Pittsburgh. The article, which appeared in *Mechanical Engineering* (May, 1955, pages 394-395), describes "a program for the development of human engineering, which deals primarily with the human factor in engineering design. Ergonomics is the basic area of applied science that is concerned with the study of human behavior in response to external stress, with particular reference to the stress-strain problems of man at work." Requests for this two page reprint should be addressed to Mellon Institute, 4400 Fifth Ave., Pittsburgh 13.

Self-Help Devices for the Arthritic Patient.—The national office of the Arthritis and Rheumatism Foundation has made a grant to implement an office for the collection, evaluation, development, and dissemination of information concerning self-help devices for the arthritic patient. The office, located in the Institute of Physical Medicine and Rehabilitation of New York University-Bellevue Medical Center, will be under the direction of Dr. Edward W. Lowman. The primary purpose of the office is to provide, without cost, information on self-help devices and to offer free consultation to arthritic patients by mail, telephone, or personal interview. Patients or physicians who have developed self-help devices are urged to submit them for testing and evaluation. The office may be reached on Mondays and Wednesdays, between 9 a. m. and 5 p. m. Telephone MUrray Hill 6-1842, ext. 85, in New York City.

Oak Ridge Participation Program.—Applications are open to college and university faculty members for places in the Oak Ridge Research Participation Program for 1956, administered by the Oak Ridge (Tenn.) Institute of Nuclear Studies in cooperation with the Oak Ridge National Laboratory. The program is designed to disseminate scientific and technical information to educational institutions by enabling faculty members to spend varying amounts of time—usually the three summer months—conducting research in Oak Ridge laboratories. The participant's Oak Ridge salary approximates his university salary. Applications for three-month summer appointments should be in the hands of the University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn., by Dec. 15. Information may be obtained from the University Relations Division. Notifications of appointment will be made by Feb. 15.

Travel Awards.—The Federation of American Societies for Experimental Biology announces that some 35 travel awards (about $500 each) will be available from its International Physiological Congress Trust Fund for the congress in Brussels, July 29-Aug. 4, 1956. Applicants must not have reached the age of 35 (by July 1, 1956) nor have attained the academic rank of full professor (or its equivalent in other than academic employment). Recipients of travel awards must present papers at the congress. Application for an award is open to those working in any of the fields of the societies of the federation. Applicants for travel awards are urged to make tentative reservations for space with Foreign Services Corporation, 1624 Eye Street, N. W., Washington 6, D. C., before Dec. 25. The closing date for applications for travel awards is Dec. 15. For application forms write: Federation of American Societies for Experimental Biology, 9650 Wisconsin Avenue, Washington 14, D. C.

Aid-to-Education Plan.—Eastman Kodak Company, Rochester, N. Y., recently announced the addition to its aid-to-education program of a plan expected to cost $300,000 in 1955 and to provide financial grants to 50 privately supported colleges and universities whose graduates are employed by the company. Privately supported institutions will receive grants based on the number of their graduates who joined the company during the fifth year preceding the year in which the grants are made and who are currently employed by the company. The grants provide payments to the institutions of $500 for each year spent by an employee at the institution from which he was graduated and at which he completed a regular and established degree program at either the undergraduate or postgraduate levels. An institution must have had at least two graduates employed by Eastman Kodak Company as of Dec. 31, 1949. The cost of the company's over-all aid-to-education program, including the new plan, will total approximately $650,000 in 1955.

United Negro College Fund.—In its 1955 campaign the United Negro College Fund points out that, although the 31 privately supported, fully accredited member colleges and universities of the fund have offered premedical training to 90% of all Negro physicians, as well as a majority of medical technicians, at present there is only one Negro physician per 4,000 Negro population. The fund's member colleges are located in 11 southern states. Since the students of these 31 accredited colleges can pay only 41.2% of the cost of their education, as against the national average of 69.1%, their tuition fee averages only $631. The United Negro College Fund appeals for contributions to secure the remaining 10% of the combined educational budgets of the colleges—$1,750,000 this year. Gifts may be made payable to the United Negro College Fund in the donor's community or may be sent to the national headquarters, 22 E. 54th St., New York, where they will be credited to the city in which the donor lives or in which his company does business. Contributions are deductible for income tax purposes.

Graduate Science Fellowships.—The National Science Foundation offers more than 750 fellowship awards for a year of graduate scientific study during the academic year 1956-1957 in connection with its fifth annual graduate fellowship program. Applications may be obtained from the Fellowship Office, National Research Council, Washington 25, D. C. The closing dates for receipt of applications are Dec. 19 for postdoctoral applicants and Jan. 3, 1956, for graduate students working toward advanced degrees in science. The selections will be announced March 15, 1956. National Science Foundation

fellowships are awarded to American citizens who will begin or continue their studies at the graduate level in the mathematical, physical, biological, medical, engineering, and other sciences during the 1956-1957 academic year. About 80 awards will be made to postdoctoral applicants. Such applicants will not be required to take examinations. Annual stipends for National Science Foundation fellowships vary with the academic status of the fellows: first year fellows—students entering graduate school for the first time or those who have had less than one year of graduate study, $1,400; fellows who need one final academic year of training for the doctor's degree, $1,800; fellows between these groups, $1,600 annually; postdoctoral fellows, $3,400. Dependency allowances will be made to all married fellows. Tuition and laboratory fees and limited travel allowances will also be provided. National Science Foundation fellows may attend any accredited nonprofit institution of higher education in the United States or similar institutions abroad.

Society News.—At the 44th annual meeting of the **International Association of Medical Museums** in Houston, Texas, April 5-6, the name of the association was changed to the **International Academy of Pathology.** The next meeting of the organization will be held in Cincinnati, April 24-25, 1956. For information, write to the secretary-treasurer, Dr. Fathollah K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C.——Newly elected officers of the **American Orthopaedic Association** include: Dr. Paul C. Colonna, Philadelphia, president; Dr. Charles R. Rountree, Oklahoma City, vice-president; Dr. David M. Bosworth, New York, president-elect; Dr. Mather Cleveland, New York, treasurer; and Dr. George O. Eaton, Baltimore, secretary.——Newly elected officers of the **Society of Biological Psychiatry** include: Dr. Howard D. Fabing, Cincinnati, president; Dr. Margaret A. Kennard, Vancouver, B. C., Canada, first vice-president; Dr. Louis J. Karnosh, Cleveland, second vice-president; and Dr. George N. Thompson, Los Angeles, secretary-treasurer.——Newly elected officers of the **Society for Pediatric Research** include: Dr. Wolfgang W. Zuelzer, Detroit, president; Dr. Nathan B. Talbot, Boston, vice-president; and Dr. Sydney S. Gellis, Boston, secretary-treasurer.——The **American Association for Thoracic Surgery** recently elected Dr. Richard H. Meade, Grand Rapids, Mich., president; Dr. Cameron Haight, Ann Arbor, Mich., vice-president; Dr. Julian Johnson, Philadelphia, treasurer; and Dr. Paul C. Samson, Lafayette, Calif., secretary. The 1956 meeting will be held in Miami Beach, Fla., May 7-9.——At the annual meeting of the **Neurosurgical Society of America,** Dr. Charles E. Troland, Richmond, Va., was elected president; Drs. Eben Alexander, Winston-Salem, N. C., and Claude M. Bertrand, Montreal, Canada, vice-presidents; Dr. Lester A. Mount, New York, secretary; and Dr. I. Joshua Speigel, Chicago, treasurer.——The **American College of Cardiology** recently installed Dr. Walter S. Priest, Chicago, as president; Dr. Simon Dack, New York, was elected president-elect; Drs. J. Maxwell Chamberlain, Seymour Fiske, New York, and John C. Scott Jr., Philadelphia, vice-presidents; and Dr. Philip Reichert, Empire State Building, New York 1, secretary-treasurer.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

1956 Annual Meeting, Chicago, June 11-15.

1956 Clinical Meeting, Seattle, Nov. 27-30.

1957 Annual Meeting, New York, June 3-7.

1957 Clinical Meeting, Philadelphia, Dec. 3-6.

NATIONAL MEDICAL PUBLIC RELATIONS CONFERENCE, Hotel Statler, Boston, Nov. 28. Mr. Leo F. Brown, 535 N. Dearborn St., Chicago 10, Director.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Palmer House, Chicago, Dec. 3-8. Dr. James R. Webster, 55 East Washington St., Chicago 2, Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Conrad Hilton Hotel, Chicago, Dec. 13. Dr. C. Paul Hodgkinson, 116 South Michigan Blvd., Chicago, Secretary.

AMERICAN ASSOCIATION OF BLOOD BANKS, Palmer House, Chicago, Nov. 19-21. Miss Marjorie Saunders, 3707 Gaston Ave., Dallas 10, Texas, Secretary.

AMERICAN LEAGUE AGAINST EPILEPSY, Roosevelt Hotel, New York, Dec. 8. Dr. Peter Kellaway, Baylor University College of Medicine, Houston 25, Tex., Secretary.

AMERICAN RHEUMATISM ASSOCIATION, Interim Session, National Institutes of Health, Bethesda, Md., Dec. 9. Dr. Edward F. Hartung, 580 Park Ave., New York 21, Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 9-10. Dr. Clarence C. Hare, 710 West 168th St., New York 32, Secretary.

EASTERN SECTION, AMERICAN FEDERATION FOR CLINICAL RESEARCH, Hotel Warwick and College of Physician's Building, Philadelphia, Dec. 2-3. Dr. Charles R. Shuman, Temple Univ. Hospital, Broad and Ontario Sts., Philadelphia 40, Chairman.

EASTERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Boston, Jan. 13. Dr. John A. Murtagh, Dartmouth College, Hanover, N. H., Vice President.

LOS ANGELES MIDWINTER MEDICAL CONVENTION, Biltmore Hotel, Los Angeles, Jan. 3-5. Dr. Paul D. Foster, 1925 Wilshire Blvd., Los Angeles 58, General Chairman.

MEDICAL SOCIETY EXECUTIVES CONFERENCE, Parker House, Boston, Nov. 27. Mr. H. Martin Baker, 1102 South Hillside, Witchita 17, Kansas, Secretary.

NEW ENGLAND HEALTH EDUCATION ASSOCIATION, Boston, Dec. 2. Miss Wyntha Tompkins, Middlesex Health Association, Essex, Mass., Secretary.

PUERTO RICO MEDICAL ASSOCIATION, Santurce, Dec. 7-11. Dr. Luis R. Guzman-Lopez, Box 9111, Santurce, Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Palmer House, Chicago, Dec. 11-16. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:

BALTIMORE, Nov. 19. Dr. R. Carmichael Tilghman, 6 East Eager St., Baltimore 2, Governor.

VANCOUVER, B. C., Nov. 19. Dr. H. A. DesBrisay, 925 West Georgia St., Vancouver, B. C., Governor.

DETROIT, Dec. 3. Dr. H. Marvin Pollard, 1313 East Ann St., Ann Arbor, Mich., Governor.

HOT SPRINGS, ARK., Dec. 3. Dr. A. A. Blair, 100 S. 14th St., Ft. Smith, Ark., Governor.

WINSTON-SALEM, N. C., Dec. 8. Dr. Elbert Persons, Duke Hospital, Durham, N. C., Governor.

SOUTHERN SURGICAL ASSOCIATION, The Homestead, Hot Springs, Va., Dec. 6-8. Dr. George G. Finney, 2947 St. Paul St., Baltimore 18, Secretary.

SOUTHERN THORACIC SURGICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, W. Va., Dec. 2-5. Dr. Hawley H. Seiler, 442 West Lafayette St., Tampa 6, Fla.

WESTERN SURGICAL ASSOCIATION, Olympic Hotel, Seattle, Dec. 1-3. Dr. John T. Reynolds, 612 N. Michigan Blvd., Chicago 11, Secretary.

FOREIGN AND INTERNATIONAL

ALL INDIA MEDICAL CONFERENCE, Jaipur, India, Dec. 26-28. Dr. B. N. Consul, Association Bldg., S.M.S. Hospital Premises, Jaipur, India, Organizing Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, Apr. 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Statler, Boston, Mass., U.S.A., Sept. 3-8, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF INTERNATIONAL SOCIETY FOR RESEARCH ON ANESTHESIA, Miami Beach, Fla., U.S.A., Mar. 12-15, 1956. For information write: Dr. R. J. Whitacre, 13951 Terrace Road, Cleveland 12, Ohio, U. S. A.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B_{12}, Hamburg, Germany, May 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF BLOOD TRANSFUSION, Boston, Mass., U. S. A., Aug. 29-Sept. 2, 1956. Dr. J. Julliard, 57, Boulevard L'Auteuil, Boulonge-sur-Seine, France, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956, Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF PHYSIOPATHOLOGY OF ANIMAL REPRODUCTION AND ARTIFICIAL INSEMINATION, Cambridge, England, June 25-29, 1956. For information address: Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

LATIN AMERICAN CONGRESS OF PATHOLOGY, Mexico, D. F., Mexico, Dec. 11-17. For information address: Laboratorio de Anatomia Patologica, Instituto N. de Cardiologia, Avenida Cuauhtemoc 300, Mexico 7, D. F., Mexico.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, New York, U. S. A., Executive Director.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-23, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Horsfall, P.O Box 672, Cairns, N.Q., Australia, Secretary.

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE, San Juan, Puerto Rico and Curacao, N.W.I., Jan. 29-Feb. 8, 1956. Dr. Arturo Martinez, 54 East 72d St., New York 21, New York, U. S. A., Secretary.

PAN AMERICAN CONGRESS OF GASTROENTEROLOGY, Havana, Cuba, Jan. 20-27, 1956. For information address: Dr. Norberto M. Stapler, 1267 J. E. Uriburu, Buenos Aires, Argentine, S. A.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Santiago, Chile, S. A., Jan. 9-14, 1956. Dr. Rene Contardo, Huerfanos 930, Of. 74, Santiago, Chile, Secretary General.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, March 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce, Puerto Rico, Secretary General.

PAN AMERICAN MEDICAL WOMEN'S ALLIANCE, Santiago, Chile, March 6-13, 1956. For information address: Dr. Eva Cutright, 458 Beall Ave., Wooster, Ohio, U. S. A.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-26, 1956. For information address: Prof. G. Tesauro, S. Andrea della Dame, 19, Naples, Italy.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-15, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Various Centers, April 24-25 (Part II); June 19-20 (Parts I and II); September 4-5 (Part I). Candidates may file applications at any time but they must be received at least six weeks before the date of the examination for which application is made. New candidates should apply by formal registration; registered candidates may notify the board, indicating desired location, date and candidate number. Ex. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination* Montgomery, June 19-21. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ARIZONA:* *Examination*. Phoenix, Jan. 18-19. *Reciprocity*. Phoenix, Jan. 21. Sec., Dr. M. R. Richter, 411 Security Bldg., Phoenix.

COLORADO:* *Examination*. Denver, Dec. 6-7. Final date for filing application is Nov. 4. Exec. Sec., Mrs. Beulah H. Hudgens, 831 Republic Bldg., Denver 2.

DELAWARE: *Examination*. Dover, Jan. 10-12. *Reciprocity*. Dover, Jan. 19. Sec., Dr. Joseph S. McDaniel, Dover.

DISTRICT OF COLUMBIA:* *Reciprocity*. Washington, Dec. 12. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave. N.W., Washington 6.

FLORIDA:* *Examination*. Miami Beach, Nov. 20-21. Sec., Dr. Homer L. Pearson, 901 N. W. 17th St., Miami.

GEORGIA: *Examination and Reciprocity*. Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: *Examination and Reciprocity*. Boise, Jan. 9-11. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination and Reciprocity*. Chicago, Jan. 24-26. Supt. of Regis., Mr. Frederic B. Selcke, Capitol Building, Springfield.

INDIANA: *Examination*. Indianapolis, June. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

IOWA:* *Examination*. Des Moines, Dec. 5-7. Ex. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines.

KANSAS: *Examination and Endorsement*. Topeka, Dec. 7-8. Sec., Dr. Lyle F. Schmaus, New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination*. Louisville, Dec. 5-7. Asst. Sec., Mr. R. F. Dixon, 620 S. 3rd St., Louisville.

LOUISIANA: *Examination and Reciprocity*. New Orleans, Dec. 1-3. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

MARYLAND: *Examination*. Baltimore, Dec. 13-16. Exec. Sec., Miss Hannah A. McCarthy, 1215 Cathedral St., Baltimore 1.

MICHIGAN:* *Examination*. Ann Arbor and Detroit, June 13-15 (Tentative). Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., Lansing.

MINNESOTA:* *Examination*. Minneapolis, Jan. 18-20. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity*. Jackson, December. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson.

MONTANA: *Examination and Reciprocity*. Helena, April 3-4. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination*. Omaha, June 18-20. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

NEVADA:* *Examination and Reciprocity.* Reno, Jan. 3. Sec., Dr. G. H. Ross, 112 N. Curry St., Carson City.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Nov. 21-22. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NEW HAMPSHIRE: *Examination and Endorsement.* Concord, March 14. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW YORK: *Examination.* Albany, Buffalo, Syracuse and New York, Feb. 7-10. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 4-6. *Reciprocity.* Grand Forks, Jan. 7. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

OHIO: *Examination.* Columbus, Dec. 15-17. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA:* *Examination.* Oklahoma City, June 5-6. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, Jan. 12-14. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia, January. Acting Sec., Miss Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, Jan. 5-6. Admin. of Professional Education, Mr. Thomas B. Casey, Room 366, State Office Bldg., Providence 2.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Jan. 17-18. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TENNESSEE:* *Examination.* Memphis, Dec. 21-22. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS:* *Examination and Reciprocity.* Galveston, Dec. 1-3. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

VIRGINIA: *Examination.* Richmond, Dec. 7-9. *Reciprocity.* Richmond, Dec. 6. Final date for filing application is Nov. 21. Address the Secretary, 631 First St. S.W., Roanoke.

WEST VIRGINIA: *Examination and Reciprocity.* Charleston, Jan. 9-11. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

WISCONSIN:* *Reciprocity and Examination.* Madison, Jan. 10-12; *Reciprocity.* Madison, Spring; *Reciprocity and Examination.* Milwaukee, July 10-12. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

WYOMING: *Examination and Endorsement.* Cheyenne, Feb. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

ALASKA:* On application. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM. The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.

HAWAII: *Examination.* Honolulu, Jan. 9-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani, St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination and Reciprocity.* Tucson, Dec. 20. Sec., Dr. H. D. Rhodes, University of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, May 4-5. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

COLORADO: *Examination.* Denver, Dec. 7-8. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave. N.W., Washington 6.

MICHIGAN: *Examination.* Detroit and Ann Arbor, Feb. 10-11. Sec., Mrs. Anne Baker, 410 W. Michigan Ave., Lansing 15.

MINNESOTA: *Examination.* Minneapolis, Jan. 3-4. Sec., Dr. Raymond N. Bieter, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Jan. 10-11. Sec., Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEVADA: *Examination.* Reno, Jan. 3. Sec., Dr. Donald G. Cooney, Box 9005, University Station, Reno.

NEW MEXICO: *Examination.* Santa Fe, Jan. 15. Sec., Mrs. Marguerite Cantrell, Box 1522, Santa Fe.

OKLAHOMA: *Examination.* Oklahoma City, Mar. 30-31. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. 3; March 3; June 2, Sept. 8 and Dec. 1. Dr. Earl M. Pallett, Sec., State Board of Higher Education, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 2-3. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: *Examination.* Galveston, Dallas, and such other locations as are warranted, April. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

WISCONSIN: Milwaukee, Dec. 3. Final date for filing application is Nov. 25. Madison, Apr. 7. Final date for filing application is Mar. 30. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Monday, Nov. 28

NBC-TV, 11 a. m. to 12 noon EST. "Medical and Health News with Howard Whitman," a segment of the "Home" program.

NBC-TV, 9 p. m. EST. "Medic" presents "Glass of Fear," the story of a cartoonist who becomes a hypochondriac as a result of a mental conflict.

ABC-TV, 9:30 p. m. EST. "Medical Horizons" will originate its program from the A. M. A.'s Clinical Session in Boston. Doctors at Boston's Children's Medical Center will report on the institution's adolescent clinic.

MAGAZINES

Life, Nov. 5, 1955

"Einstein Memorial"

News and picture story reporting on dedication of the Albert Einstein College of Medicine of Yeshiva University, New York.

Saturday Evening Post, Nov. 12, 1955

"The Doctor Who Sees Through You," by Greer Williams

A profile of Harvard Medical School's Dr. Merrill C. Sosman, described by "medical admirers" as "the greatest X-ray diagnostician in America and, unquestionably, one of the greatest clinical teachers in all medicine." The article also describes the work of a radiologist.

"Operation Brotherhood," by Derrell Berrigan

In Vietnam, Indochina, a group of Filipino volunteer doctors, nurses, and dentists have banded together to provide medical assistance and treatment for residents of the war-ravaged area.

Parade, Nov. 20, 1955

"Medicine's New Weapons Against Heart Disease," by Robert P. Goldman

What most people refer to as "heart disease" actually includes more than two dozen separate illnesses. Two kinds of heart diseases, rheumatic and congenital, appear to be on the run. Two others, atherosclerosis and high blood pressure, are better treated than ever. The author tells "how we're fighting the No. 1 threat to our nation's health."

Pageant, December, 1955

"An Accurate 60-Minute Test for Pregnancy," by Turner Hodges

The writer reports that in the so-called dermal test, an injection of colostrum will cause a bump to rise on a woman's skin. If the woman is pregnant, the bump will soon disappear. If she is not pregnant, the bump will remain for several hours. According to the article, a drug firm in Los Angeles solved many of the early problems in administering the test by devising a tiny plastic device called the micro-dispenser, which contains the colostrum and a built-in needle.

"Are You Driving Your Alcoholic to Drink?" by Shirley Kessler

Al-Anon Family Groups is an organization incorporated this year as a separate entity from AA to provide guidance for families of alcoholics. It is an "experience-exchange oasis to give husbands and wives a chance for releasing tensions in talks with others who understand."

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DEATHS

Hess, Julius Hays ✙ Chicago, since 1944 professor of pediatrics, emeritus, University of Illinois College of Medicine, died of a heart attack while visiting in Los Angeles Nov. 2, aged 79. Dr. Hess was born in Ottawa, Ill., Jan. 26, 1876, and received his M.D. degree at Northwestern University Medical School in Chicago in 1899. He interned at Alexian Brothers Hospital, Chicago, and continued postgraduate work at Johns Hopkins Hospital in Baltimore and at European clinics. From 1908 to 1913 he was an instructor in pediatrics at his alma mater and in 1913 joined the faculty of the University of Illinois College of Medicine as an associate professor of pediatrics, becoming professor and head of the department of pediatrics in 1916, and serving until 1944, when he reached retirement age. Dr. Hess was a specialist certified by the American Board of Pediatrics, a fellow of the American College of Physicians, and a member of the American Pediatric Society and the American Academy of Pediatrics, which in 1952 presented him with the Borden Award "for his many productive contributions to the care and management of the prematurely born infant." In 1934-1935 Dr. Hess was president of the Chicago Medical Society and later was vice-president of the Institute of Medicine of Chicago. In 1951 he was a member of the House of Delegates of the American Medical Association, serving at one time as chairman of its Section on Pediatrics. During World War I he was a major in the Medical Corps of the U. S. Army and was commanding officer of General Hospital no. 25. He served as a member of the advisory board, Children's Bureau, Department of Labor, Washington, D. C., was a member of the Illinois Board of Welfare Commissioners, a medical member of the advisory board for Prevention of Juvenile Delinquency, a member of the medical advisory board of the Illinois Public Aid Commission, the Cook County and Chicago Welfare Administration, and the Illinois Crippled Children's Commission. For many years he was on the staff of the Englewood Hospital and consulting pediatrician and member of the executive board of the Municipal Contagious Disease Hospital. Dr. Hess was chairman of the medical committee of the Jewish Children's Bureau. He served as attending pediatrician at the Illinois Research and Educational Hospital and the Cook County Hospital, and was senior attending pediatrician at the Michael Reese Hospital, where he was head of the department, and was instrumental in the establishment of the first premature station at the Sarah Morris Hospital, a unit of Michael Reese. He devised a small hand ambulance bag to facilitate transportation of premature infants, an electrically heated water jacketed bed, and an oxygen therapy unit for premature infants. He was a founder and chairman of the medical advisory committee of the Cook County chapter, National Foundation for Infantile Paralysis. In 1955 he was one of six Chicagoans who was granted a Golden Age Hall of Fame citation for his contribution to pediatrics after reaching the age of 65. Dr. Hess contributed chapters to systems in pediatrics and he was the author of "Feeding and Nutritional Disorders of Infancy and Childhood," "Premature and Congenitally Diseased Infants," and "The Physical and Mental Development of Prematurely Born Children," and joint author with Dr. Evelyn C. Lundeen of "The Premature Infant."

Vernon, James William ✙ Morganton, N. C.; born in Person County July 21, 1886; Jefferson Medical College of Philadelphia, 1909; past-president of the Medical Society of the State of North Carolina, state board of medical examiners, Burke County Medical Society, and the North Carolina Neuropsychiatric Society; member of the Southern Psychiatric Association, American Psychiatric Association, American Ornithologists Union, American Association for the Advancement of Science, and the North Carolina Academy of Science; fellow of the American College of Physicians; mayor of Morganton from 1933 to 1937; served in France during World War I; since October, 1940, examining physician to Burke County Local Board no. 1; specialist certified by the American Board of Psychiatry and Neurology; consulting psychiatrist at the Morganton State Hospital and psychiatrist at Grace Hospital; since 1921 superintendent of the Broadoaks Sanatorium, where from 1910 to 1917 he was assistant physician; a director of the First National Bank; company surgeon to the Southern Railway; died July 16, aged 68, of cerebrovascular accident.

Fitz, Frederick William ✙ Chicago; born in Lomax, Ill., Sept. 9, 1902; Northwestern University Medical School, Chicago, 1934; associate professor of medicine at his alma mater, where he was chief of the heart and circulation clinic; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; from 1939 to 1941 first medical counselor of the Chicago *Tribune;* served in the European theater during World War II; later joined the Army's civilian consultant system and made a tour of American hospitals in the Pacific in 1948-1949; medical director of the A. B. Dick Company and the Jewel Tea Company; area consultant, Veterans Administration Hospital; member and past-president of the staff of the Passavant Memorial Hospital, where he died Oct. 8, aged 53, of coronary artery disease.

Halsey, Robert Hurtin, New York City; born in Astoria, Long Island, June 15, 1873; Columbia University College of Physicians and Surgeons, New York City, 1900; at one time professor of medicine at the New York Post-Graduate Medical School and Hospital, Columbia University; a founder of the New York Heart Association; a founder, the first secretary, and in 1932 president of the American Heart Association, which gave him one of its first gold heart awards for outstanding contributions in the fight against heart disease; member of the Harvey society, the Society for Experimental Biology, and other scientific and medical groups; an associate member of the American Medical Association; served during World War I; consultant at Goldwater Memorial Hospital; died in Stanstead, Quebec, Canada, Sept. 15, aged 82.

Boyers, Luther Musson ✙ Berkeley, Calif.; born in Decatur, Ind., March 29, 1888; Leland Stanford Junior University School of Medicine, San Francisco, 1916; during World War I served as a contract surgeon for the U. S. Army at the University of California; from 1919 to 1923 assistant physician and surgeon for men at the University of California Infirmary, where he served as research associate and consultant in parasitology; life member of the American Public Health Association; for 30 years member of the cancer research group and tumor board at his alma mater; active at the Ernest V. Cowell Memorial Hospital; died in the Stanford University Hospital Sept. 19, aged 67, of mesenteric thrombosis.

Dooley, Emmett Alfred ✙ New York City; born in Windsor Mills, Quebec, Canada, Aug. 22, 1897; Syracuse University College of Medicine, 1923; associate clinical professor of surgery at the Post-Graduate Medical School of the New York University-Bellevue Medical Center; fellow of the American College of Surgeons and the New York Academy of Medicine; governor of the American Academy of Compensation Medicine; president of the New York Catholic Physicians Guild; director of traumatic and orthopedic surgery at Columbus Hospital; consultant at the Morrisania City Hospital; died Sept. 24, aged 58, of coronary heart disease.

Williams, John Thomas ✙ Boston; Harvard Medical School, Boston, 1904; served as assistant professor of gynecology at his alma mater; in 1936 president of the Obstetrical Society of Boston; fellow of the American College of Surgeons; chief of obstetrics at the Whidden Memorial Hospital in Everett, the Chelsea (Mass.) Memorial Hospital, and the Winthrop (Mass.) Community Hospital; on the staff of the Boston City Hospital for many years, serving as surgeon-in-chief for obstetrics and gynecology from 1935 to 1943; died Sept. 18, aged 73, of myocardial infarction.

✙ Indicates Member of the American Medical Association.

Allen, Burton Watson ✦ Dallas, Texas; Baylor University College of Medicine, 1931; member of the American Academy of General Practice; died Sept. 19, aged 61, of bronchopneumonia.

Allen, Millard Fillmore ✦ New Haven, Conn.; Medico-Chirurgical College of Philadelphia, 1895; died Sept. 5, aged 100, of arteriosclerotic heart disease.

Arling, Philip Arthur ✦ McMinnville, Ore.; University of Minnesota Medical School, Minneapolis, 1941; served during World War II; died Sept. 29, aged 46, in an automobile accident.

Arnoldussen, Chris Philip ✦ Fremont, Wis.; Marquette University School of Medicine, Milwaukee, 1937; died in New London (Wis.) Community Hospital July 15, aged 44, of a skull fracture received in an automobile accident.

Bak, Edward William ✦ Los Angeles; Rush Medical College, Chicago, 1898; member of the staff of the Cedars of Lebanon Hospital, where he died Sept. 17, aged 80, of heart disease.

Battles, Charles Edwin, Cleveland; Cleveland Homeopathic Medical College, 1903; one of the founders of Grace Hospital, where he was a member of the initial staff; died Sept. 25, aged 78, of a heart attack.

Beatty, Mary Teresa Veronica Moore, Boston; Tufts College Medical School, Boston, 1913; member of the Massachusetts Medical Society; physician in Boston schools for many years; at one time a trustee of the city public library; an advisory trustee of the nursing school at Holy Ghost Hospital in Cambridge, Mass.; assistant superintendent, sanatorium division, Boston City Hospital; on the courtesy staff, St. Elizabeth's Hospital, where she died Sept. 4, aged 64, of arteriosclerotic heart disease with congestive failure and cancer of the breast.

Blaufuss, Armin Louis ✦ Geneva, Ill.; University of Illinois College of Medicine, Chicago, 1936; on the staffs of the Delnor Hospital in St. Charles and the Community Hospital, where he died Oct. 4, aged 52, of a heart attack.

Botsford, Charles Porter ✦ Hartford, Conn.; Yale University School of Medicine, New Haven, 1894; for many years city health officer; member of the American Public Health Association; died Sept. 6, aged 84, of coronary insufficiency.

Bridgman, Thomas Francis ✦ New York City; University of Pennsylvania Department of Medicine, Philadelphia, 1903; an associate member of the American Medical Association; died Sept. 17, aged 77.

Brooks, Robert Hartley ✦ Scarsdale, N. Y.; Harvard Medical School, Boston, 1905; member of the New Hampshire Medical Society; for many years practiced in Claremont, N. H.; died in White Plains (N. Y.) Hospital Aug. 27, aged 77, of acute myocardial infarction.

Burke, John Bennett ✦ Troy, N. Y.; Albany (N. Y.) Medical College, 1910; on the staff of St. Mary's Hospital; died Sept. 8, aged 69, of coronary thrombosis.

Bush, James Allen, Salt Lake City; University of Rochester (N. Y.) School of Medicine and Dentistry, 1947; instructor in pediatrics at the University of Utah College of Medicine; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pediatrics; interned at the Strong Memorial Hospital in Rochester, N. Y.; served a residency at the Salt Lake County General Hospital, Presbyterian Hospital, New York City, and Trudeau (N. Y.) Sanatorium; from 1950 to 1952 an officer in the Medical Corps of the U. S. Naval Reserve; killed in an airplane crash Oct. 6, aged 31.

Carter, Robert Lee ✦ Church Hill, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1913; died in Johnson City July 21, aged 78, of coronary thrombosis.

Ceytlin, Benjamin Herman, New York City; Uniwersytet Jozefa Pilsudskiego, Warszawa, Poland, 1927; member of the Medical Society of the State of New York; served on the staff of the Manhattan State Hospital; assistant attending physician at the New York University-Bellevue Medical Center; died in the Flower and Fifth Avenue Hospital Sept. 19, aged 54, of metastatic melanoma.

Chauss, Jay Manuel ✦ Toledo, Ohio; University of Minnesota Medical School, Minneapolis, 1948; specialist certified by the American Board of Radiology; member of the Medical Society of the State of New York; on the staff of the Maumee Valley Hospital; died Sept. 16, aged 30.

Chesson, Andrew Long ✦ Raleigh, N. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1936; served during World War II; drowned in Chesapeake Bay, North Beach, Md., Aug. 12, aged 41.

Colt, James Dennison ✦ Manhattan, Kan.; University Medical College of Kansas City, 1900; also a graduate in pharmacy; member of the House of Delegates of the American Medical Association from 1933 to 1935; served as vice-president and director of the Union National Bank; on the honorary staff of St. Mary Hospital, where he died Aug. 30, aged 88, of cerebral hemorrhage.

Corwin, Charles T. ✦ Chicago; Northwestern University Medical School, Chicago, 1906; died in the Evangelical Hospital Sept. 24, aged 79, of cerebral thrombosis.

Creekmur, Roger Lee ✦ Richmond, Va.; Medical College of Virginia, Richmond, 1921; for many years physician and surgeon for the city fire bureau; served on the staffs of the Stuart Circle Hospital, Retreat for the Sick, and Medical College of Virginia Hospital; died Sept. 3, aged 59, of a heart attack.

Crisp, Sellers Mark ✦ Greenville, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1923; died July 20, aged 60, of coronary occlusion.

Culp, Earle E., Chicago; Missouri Medical College, St. Louis, 1896; died Sept. 10, aged 80, of coronary thrombosis.

Davidson, Herman Porter ✦ Chicago; Johns Hopkins University School of Medicine, Baltimore, 1917; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Chicago Memorial and Presbyterian hospitals; died in St. Luke's Hospital Oct. 9, aged 64, of hypertensive encephalopathy.

Dennison, John Chase ✦ Bellevue, Iowa; State University of Iowa College of Medicine, Iowa City, 1889; also a graduate in pharmacy; past-president of the Jackson County Medical Society; for many years health officer; served during World War I; later a major in the Medical Reserve Corps; was president of the Bellevue Telephone Company and the Bellevue Clay Products Company; served on the city council and school board; died in the Bellevue Memorial Hospital Sept. 21, aged 89, of cerebral hemorrhage.

DuPuis, John Gordon ✦ Miami, Fla.; Hospital College of Medicine, Louisville, Ky., 1898; died Sept. 17, aged 79, of coronary thrombosis.

Fitzsimmons, Elvin Lee ✦ Evansville, Ind.; Indiana University School of Medicine, Indianapolis, 1935; specialist certified by the American Board of Proctology; past-president of the Vanderburgh County Medical Society; served during World War II; on the staffs of St. Mary's, Protestant Deaconess, and Welborn Memorial Baptist hospitals; died in the Barnes Hospital, St. Louis, Aug. 22, aged 44, of a brain tumor.

Freda, Leonard Aloysious ✦ Dunmore, Pa.; Temple University School of Medicine, Philadelphia, 1920; served during World War I; formerly county coroner; fellow of the International College of Surgeons; active in athletics, and held the post of regional medical examiner for the Pennsylvania State Athletic Commission; for many years associated with the Scranton (Pa.) State Hospital, where he was superintendent from January, 1944, to August, 1954; died in the Mercy Hospital in Scranton July 15, aged 60.

Gallaher, David Mars ✦ Appleton, Wis.; State University of Iowa College of Medicine, Iowa City, 1923; fellow of the American College of Surgeons; served during World War I; for many years member and at one time president of the library board; on the staff of St. Elizabeth Hospital, where he died July 30, aged 59, of virus pneumonia, hemiplegia, and Alzheimer's disease.

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Gaster, Emil, Brooklyn, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1920; member of the Medical Society of the State of New York; died Sept. 8, aged 69, of coronary occlusion.

Graham-Rogers, Charles T., Ridgefield, Conn.; Baltimore University School of Medicine, 1899; served during World War I; for many years associated with the New York State Department of Labor; member of the Industrial Medical Association and the Medical Society of the State of New York; an associate member of the American Medical Association; died Sept. 24, aged 81.

Hathaway, Robert Joseph, Glendive, Mont.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; fellow of the American College of Surgeons; served during World War I; died July 15, aged 81, of probable coronary occlusion.

Held, Louis Arthur ✦ Brooklyn, N. Y.; University and Bellevue Hospital Medical College, New York City, 1914; specialist certified by the American Board of Radiology; instructor in radiology at the New York Post Graduate Medical School from 1921 to 1923; attending radiologist at the Beth Moses Hospital from 1925 to 1948, when he became attending radiologist at the Maimonides Hospital; died Sept. 20, aged 62, of coronary occlusion.

Hill, Garland Withers, Cleveland, Tenn.; Atlanta College of Physicians and Surgeons, 1902; died in the Veterans Administration Hospital, Murfreesboro, July 7, aged 75, of a heart attack.

Hines, Brainard Evans ✦ Charleston, W. Va.; Medical College of Virginia, Richmond, 1939; served during World War II; resident of the Mountain State Memorial Hospital; on the associate staff of St. Francis Hospital, where he died Oct. 2, aged 42, of pulmonary embolism and thrombophlebitis of the leg.

Hoge, Myrvin Eugene ✦ Jackson, Ky.; Kentucky School of Medicine, Louisville, 1904; president of the Breathitt County Medical Society; member of the county board of health; trustee of the Lees Junior College; died Sept. 8, aged 75.

Holmes, Colin McLean ✦ Springfield, Mass.; College of Physicians and Surgeons, Baltimore, 1915; died Aug. 10, aged 68, of adenocarcinoma of the sigmoid.

Horning, William H. ✦ York, Pa.; Jefferson Medical College of Philadelphia, 1902; died July 27, aged 78, of cerebral accident.

Johnstone, Alexander Anthony ✦ Keokuk, Iowa; State University of Iowa College of Medicine, Iowa City, 1928; fellow of the American College of Surgeons; served during World War II; on the staffs of the Graham Protestant and St. Joseph's hospitals; died Aug. 5, aged 57, of cancer.

Kasboum, William J., Houston, Texas; University of Buffalo School of Medicine, 1939; served during World War II; died in the Veterans Administration Hospital Sept. 2, aged 46, of carcinoma of the lung.

Keating, Charles V. ✦ Beacon, N. Y.; Jefferson Medical College of Philadelphia, 1909; chairman of draft boards in the Beacon area during World Wars I and II; chief of staff at Highland Hospital; died Sept. 5, aged 70.

Kennedy, Robert Walden ✦ Marshall, Mo.; University of Louisville (Ky.) School of Medicine, 1920; member of the American Academy of General Practice; on the staffs of the Georgia Brown Blosser Home for Crippled Children and the John Fitzgibbon Memorial Hospital; died Aug. 14, aged 62, of coronary occlusion.

Kenyon, Paul E., Vestal, N. Y.; Northwestern University Medical School, Chicago, 1896; served in France during World War I; died Sept. 17, aged 86.

Kerr, James Purdy, Pittsburgh; University of Maryland School of Medicine, Baltimore, 1888; an associate member of the American Medical Association; fellow of the American College of Surgeons; served as president of the city council; on the staff of St. Joseph's Hospital, where he died Sept. 9, aged 91, of arteriosclerotic heart disease.

Lucas, Peter Joseph, Amsterdam, N. Y.; Georgetown University School of Medicine, Washington, D. C., 1936; member of the Medical Society of the State of New York and the American Academy of General Practice; served as county coroner; on the staffs of the Amsterdam Hospital and St. Mary's Hospital, where he died Sept. 3, aged 45, of acute enteritis.

Lutton, Ethelbert Arnold ✦ Chicago; Northwestern University Medical School, Chicago, 1918; member of the International College of Surgeons; on the staff of the South Shore Hospital; died in the Albert Merritt Billings Hospital Oct. 1, aged 62, of bronchogenic carcinoma with metastases.

Nelson, Frederick Lawrence ✦ Ottumwa, Iowa; University and Bellevue Hospital Medical College, New York City, 1903; member of the International College of Surgeons; fellow of the American College of Surgeons; at one time on the faculty of Fordham University School of Medicine in New York City, where he was on the staff of the Lincoln Hospital; served during World War I; on the staffs of the Ottumwa and St. Joseph hospitals; consultant in surgical urology, Sunnyslope Sanatorium; instantly killed in an automobile accident Oct. 1, aged 77.

Schutz, Leopold, Chicago; Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau, Prussia, Germany, 1917; on the staff of the Southtown Hospital; died Sept. 6, aged 68, of heart disease.

Shaul, Frederick Gersham ✦ Bloomfield, N. J.; Baltimore Medical College, 1901; an associate member of the American Medical Association; attending surgeon, emeritus, Newark (N. J.) Eye and Ear Infirmary; died Sept. 13, aged 77, of dissecting aneurysm of the aorta.

Shreck, John Addison ✦ Redlands, Calif.; Rush Medical College, Chicago, 1891; an associate member of the American Medical Association; served during World War I; served as director of the Holton Power Company, First National Bank of Redlands, and the Chapman College in Los Angeles; for many years on the staff of the San Bernardino (Calif.) County Charity Hospital; died in the Redlands Community Hospital Sept. 3, aged 91.

Skwirsky, Joseph ✦ Newark, N. J.; University and Bellevue Hospital Medical College, New York City, 1923; specialist certified by the American Board of Internal Medicine; member of the American Academy of Allergy, American Diabetes Association, and the Academy of Medicine of New Jersey; past-president of the New Jersey Diabetic Association; on the staff of the Beth Israel Hospital, where he served an internship, and where he died Sept. 15, aged 62, of myocardial infarction and diabetes mellitus.

Treister, Bert Allen, Cleveland Heights, Ohio; Western Reserve University School of Medicine, Cleveland, 1932; member of the Ohio State Medical Association, Cleveland Academy of Medicine, and the American Society of Physical Medicine; specialist certified by the American Board of Physical Medicine and Rehabilitation; served during World War II; on the staff of St. Vincent Charity Hospital in Cleveland; died in the University Hospital, Cleveland, Sept. 21, aged 46, of coronary thrombosis.

Turner, Edmond Daniel ✦ Cave City, Ky.; Hospital College of Medicine, Louisville, 1906; twice president of the Barren County Medical Society; served during World War I; died in Glasgow Sept. 17, aged 81, of coronary thrombosis.

Walter, Will, Charlottesville, Va.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; specialist certified by the American Board of Ophthalmology; fellow of the American College of Surgeons; formerly practiced in Evanston, Ill., where he was on the staff of the Evanston Hospital; died in October, aged 88.

Whitehill, James Lorrin ✦ Rochester, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1923; member of the House of Delegates of the American Medical Association from 1948 to 1954; past-president of the Medical Society of the State of Pennsylvania; served during World War I; chief of urology and president of the staffs of the Rochester General Hospital in Rochester, the Beaver Valley General Hospital at New Brighton, and the Providence Hospital in Beaver Falls; died Sept. 13, aged 58.

FOREIGN LETTERS

ENGLAND

Congress of Neuropathology.—At the second International Congress of Neuropathology, held in London in September, Dr. W. Blackwood of London described the findings in cortical biopsy specimens from 30 children with progressive dementia. In about half it was possible to indicate the pathological process, and in about a third to give a precise diagnosis. Drs. S. W. McMenemey and S. Nevin (London) described five further cases of a condition described by Nevin in 1954, the characteristic features of which were signs of focal cerebral disorder, such as clouding of consciousness, hemiplegia, mental disturbances, and myoclonic epilepsy occurring in later adult life. This was progressive and fatal within a few months. The electroencephalogram changes were characteristic; namely, periodically recurring, generalized, sharp, and slow wave complexes. The lesions were also distinctive—widespread cortical degeneration and glial reaction and a tendency to status spongiosus. In another discussion tentorial herniation was considered as a possible cause of temporal lobe epilepsy, which could be caused by ischemia of the compressed parts of the temporal lobe and subsequent scarring, the scar acting as an epileptic focus. Various vessels could also get compressed in the hernia. Dr. H. Pia (Gieseen, Germany) explained some vascular lesions of the occipital lobes on the basis of compression of vessels against the tentorial border. Dr. L. Wolman (Sheffield) analyzed the findings in 270 patients dying with a tentorial pressure cone: 12% showed hemorrhagic infarction of the occipital lobes and 5% infarction of the pituitary gland. Drs. J. Cavanagh and A. Meyer (London) described the results of changes seen in 40 resected temporal lobes. In 10 there were single focal lesions due to tumors, vascular malformation, or trauma; in most of the remainder, the lesions were diffuse or disseminated. The possibility of birth injury could not be excluded in some.

At a session on encephalitis, Dr. K. Kristiansen and his colleagues (Oslo, Norway) stated that acute hemorrhagic encephalitis was not necessarily fatal. The condition might be diagnosed in life by necrosis, cellular infiltration, hemorrhage, and demyelination in biopsy specimens. Of six patients studied, three survived, two with mental symptoms. Dr. M. Gozzano and his co-workers (Rome, Italy) described experiments to illustrate the efficacy of streptomycin in the treatment of experimental tuberculous encephalitis in guinea pigs. Treatment of inoculated animals with 30 mg. of streptomycin intramuscularly and brain tissue daily resulted in survival of the animals for six months. The controls all died within a week. It was not clear how the brain tissue acted. In the section on trauma, Dr. C. Benda (Waverley, Mass.) said that the effect of a single cranial injury was not restricted to the event, but was progressive, and led to interference with the circulation and nutrition of the brain. In infancy and childhood trauma might distort subsequent brain development. The late effects of trauma due to anoxia were described by Dr. A. Løken (Oslo, Norway). A youth, aged 18, survived four and a half years in a state of decerebration after a 10 minute arrest of heart and respiration. He lay most of the time with open eyes, although blind, and responded to strong auditory and painful stimuli with slow muscular movements. The parieto-occipital lobes and frontal gyri were severely damaged and the thalami were small and shrunken. Dr. S. Strich (Oxford) mentioned five patients with cranial injury, uncomplicated at the time, resulting in severe dementia until death 5 to 15 months later. Within three weeks of injury the patients were immobile with severe bilateral spastic hemiplegia, incontinence, and aphasia. Macroscopic changes in the brain were not pronounced, but microscopy showed widespread degeneration of white matter, loss of nerve fibers, and atrophy of the thalamus. Dr. R. Lindenberg and co-workers (Baltimore, Md.) described the pathological findings in 57 infants and children with cranial injuries due to blunt agents. The frequency of contusional foci was low in infants and the frequency rose with age. In the soft brains of infants small hemorrhagic tears were sometimes seen in the subcortical white matter. Death was usually due to severely increased intracranial pressure, which reached a critical level 15 to 20 minutes after the accident. Drs. D. Wollam and J. Millen (Cambridge) said that there were four possible sites for the blood-brain barrier—the capillary endothelium, the neuroglia, the ground substance, and the neuron itself. Dr. J. Gruner (Paris, France) said that radioactive isotope studies had shown that different substances passed through the blood-brain barrier at a variable speed; the all-or-none law did not apply. Water, oxygen, and anesthetics passed through so quickly that exact measurement was impossible; large molecules and toxins did not pass at all. The velocity and degree of passage varied with the region of the brain. They were greatest in the choroid plexuses, the posterior hypophysis and the epiphysis, and the hypoependymal organs. Dr. T. Broman (Göteborg, Sweden) showed that pial vessels behaved like cerebral capillaries in their impermeability to dyes, and he argued that part at least of the blood-brain barrier is in the capillary wall.

British Greenland Expedition.—A British expedition to northern Greenland was sponsored in 1952 by the Royal Society, the Medical Research Council, the Royal Geographical Society, and the armed services, the object being to study the geology, geophysics, and meterology of the region and the medical, physiological, and nutritional aspects of exploration in arctic regions. The explorers remained in North Greenland from 1952 to 1954. Lewis and Masterton report on the medical aspects of the expedition (*Lancet* **2**:549, 1955). All food was brought from Britain and consisted of canned meat, vegetables, fruit, and dried foods, such as cabbages, potatoes, carrots, and onions. It was found that many products such as whole potatoes and root vegetables, eggs, bacon, salted meat, cheese, and sausage would have kept perfectly in ice, which is present even in summer in northern Greenland. Bottled products were kept indoors owing to the danger of freezing and cracking.

Every member of the team carried a personal first-aid kit of 2 ampuls of morphine, 2 assorted elastoplast dressings, a field dressing such as is used in the armed services, a crepe bandage, sulfanilamide powder, and lanolin. Each unit was equipped with an extensive first-aid kit. A laboratory was fitted up at the base for physiological and medical research. Distilled water was obtained by heating ice in gasoline cans with a primus stove and condensing the steam outside the hut (temperature −39 F). Laboratory ware was made of polythene, not glass, wherever possible to prevent cracking. Among the problems investigated were sleep rhythm, which was expected to change under arctic conditions, diurnal temperature, physical efficiency as determined with the Harvard Pack Test, changes in weight, variations in the thickness of the fat layers of the body, and basal metabolic rate. Hematological studies included examination of red blood cell count, hematocrit, and hemoglobin to see if these were subject to seasonal changes. Eosinophil counts were also made as an assessment of stress, and specimens of blood for cholinesterase estimation were brought back. The caloric value of the diet of a group of men was carefully measured while they were at base and later during sledging expeditions. Specimens of total feces were brought back so that a complete analysis of the nutritional balance could be made. Blood and feces specimens were preserved in the ice in winter or in lingering snow drifts in summer. Fluid intake and output in summer and winter and at rest and exercise were compared.

The medical problems encountered were mainly cold injury, trauma, and unexpected illnesses. Snow blindness was not encountered and frostbite was rare, as precautions were taken against these. Traumatic conditions were few and included fractured ribs and ankles and a death from a fall of 300 ft. Over the two year period a long list of unexpected conditions was encountered. Among the more serious conditions were filariasis,

The items in these letters are contributed by regular correspondents in the various foreign countries.

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malaria, asthma, cardiospasm, pruritus, amblyopia, persistent headache, and petit mal seizures. Some of these might have been avoided by better medical screening of personnel before departure. Nine had recurrent upper respiratory infections, but the common cold did not occur, except from association with relief parties who brought in the infection from outside. Among other conditions occurring were herpes zoster, lumbago, supraspinatus tendinitis, dermatophytosis of the feet, chronic blepharitis, sycosis barbae, dandruff, and ingrowing toenails. There were also some anxiety states. Dentistry presented one of the biggest problems. A foot-operated dental machine was taken along, and it was necessary to make 45 fillings. After some trial it was found that gutta-percha was the most satisfactory filling material. Seven dental extractions were done under local analgesia. It was difficult to be sure whether caries were accelerated by the Arctic conditions, but the impression gained was that it was not. Throughout the two years the two physicians in the team were in radio communication with medical advisers in Britain.

Nation's Health.—The annual report for England and Wales by the Ministry of Health (Report of the Ministry of Health for the Year Ended Dec. 31, 1954: Part I. 1. The National Health Service. 2. Welfare Foods and Drugs, Civil Defense, Cmd. 9566, London, Her Majesty's Stat. Off., 1955) shows that in 1954 the cost of the National Health Service was $1,324,400,000, or about $317 a head. Although general medical services—i. e., those rendered by general practitioners—were only a fifth of the cost of hospital and specialist services, if efficiently run these general medical services could save many patients from going to the hospital. There was a decrease of a million in the annual number of prescriptions issued, but, even so, each person in the country received an average of five prescriptions at a cost of $3 per person. In 1948 when the service was introduced the average cost of a prescription was 35 cents; now it is 62 cents. The number of free hearing aids issued from 1948 to the end of 1954 was 412,000.

The total number of full-time and part-time specialists in the service showed an increase of 1.6% over 1953. The numbers in certain specialties such as ophthalmology and venereology were static, while others, particularly in anesthesiology, showed an extensive rise. There were 6,899 general practitioners working alone in the service in the middle of last year, a decline of 248 since 1953, and 11,583 working in partnership. Most of the 1,500 assistants to general practitioners were 30 years of age or under, although 45 were over 65. There is a trend for more physicians to practice in partnership. In London 48% of patients are on lists of less than 2,500 patients, and 52% are on larger lists. In Norwich, a small city, only 20% are on the smaller lists and 80% on the larger, but in Bournemouth, a prosperous resort town, 84% are on lists under 2,500. The minister complains that there is too high a concentration of physicians in London and the South. In 1954 the waiting list for hospital admission decreased by 49,000 to 474,000, a reduction of about 10%. The number of hospital inpatients increased by 87,000 in 1954. There was an improved turnover in the use of beds due to shorter stay in the hospital. The number of beds allotted to general practitioners has been stationary for the last five years, and the number of private beds has dropped by 500. The average stay in the hospital depended on the specialty involved. The stay for ear, nose, and throat operations averaged 8.1 days; for gynecologic conditions 11.5 days; and for diseases of the chest 151.7 days. The work done in radiological departments for general practitioners rose by 5% and in pathology departments by 7.5%. In the last year 28 million dollars was allocated to the hospitals for capital development, bringing the total since the introduction of the National Health Service to $141,400,000. The mental health services are still overcrowded and overworked, but nothing has been done to build or extend hospitals or to remedy the shortage of nurses for the mentally ill. The number of reported cases of tuberculosis decreased, although there were better diagnostic facilities. Waiting lists for treatment of tuberculous patients were reduced from 10,986 in 1948 to 3,017 in 1954.

The number of physicians against whom it was necessary to take disciplinary action was low. Two were removed from the service, fines were imposed on 77, a warning letter was sent to 44, and some other action was taken against 9. Claims for negligence against hospitals reached a peak in 1954, $435,332 being paid out in damages. This sum does not include legal costs. There is no evidence that there has been any deterioration in the standard of service. The rising number of claims is due to the legal ruling that the hospital is responsible for the negligence of its servants, the provision of free legal aid, and the attitude of the litigious patient who aims to get all he can out of the state.

Rehabilitation of the Tuberculous Patient.—In its annual report (Cmd. 5522, London, Her Majesty's Stat. Off., 1955) the Ministry of Labour and National Service states that in Great Britain there are 835,473 disabled persons on the register. Of these, 4,000 have completed vocational training; industrial rehabilitation has provided for 10,000; and over 115,000 have been placed in ordinary employment. Tuberculous subjects number 67,108 on the disability register, and, of these, 55,812 have respiratory tuberculosis. The rehabilitation of these people is discussed by Dr. Kenneth Marsh (*M. Officer* **94**:31, 1955). A part-time course in aero detail, fitting for tuberculous patients, was begun as an experiment in one of the London government training centers. This course gives patients with quiescent lesions an opportunity for four hours' work daily for 12 months. Awards were made to 233 tuberculous patients for professional training in the last year. For tuberculous patients who need work under sheltered conditions, Remploy Ltd. reserves seven factories, which employed 525 people in 1954. Five approved village or special workshops have been set up by voluntary bodies or local authorities. The Ministry of Labour grants financial assistance toward the maintenance and training of the patients from the stage when they can only work a few hours daily to the time when they can do a full day's work. Local education authorities will provide home instruction to groups of eight people at a time, but it is not easy to find eight people for such instruction in the same area at a given time. Homework is done sometimes by the tuberculous patient, but it is always piecework. To obtain a decent living in this way the patient must often work harder than he should or the rest of the family must help. Homework provided by Remploy Ltd., however, bears on the work in the factory to which the patient hopes to return. Remploy Ltd. factories will accept patients in whom sputum is positive, but few others will.

The Ministry of Labour rehabilitation units do not accept patients with a positive sputum, and those accepted at government training centers have to be capable of full employment. Dr. Marsh believes that colonies for tuberculous patients are outdated, as there they do not lead a normal life because they are too sheltered. Of almost 2,000 patients on the Camberwell Chest Clinic Register, 555 were capable of working and 460 of these were in full-time employment; 23 were working part time; and 75 were unemployed. Of the fully employed group, 3 had a positive sputum and 16 were in unsuitable occupations. Sheltered workshops for 2,510 patients in whom sputum is positive and retraining schemes for 3,780 with closed cases of tuberculosis are needed. These schemes can only be run at a loss. Patients with positive sputum must be kept away from their fellow workers—preferably in sheltered workshops employing small numbers. Some adequate form of family allowance would help to insure the adequate nutrition of the patient and his or her family and protect them from infection.

Legal Responsibility of Physicians.—An editorial (*Lancet* **2**:599, 1955) states that in the eyes of the law both senior surgeon and the junior boilerman are servants of the hospital authority, which now assumes responsibility for the care of its patients and the actions of all its employees. The law now takes no account of the difference in status between professional and nonprofessional workers in hospitals. This view is generally unacceptable to physicians because patients are not cared for by committees, boards, or ministers. There was a hope that the law would follow the Scottish practice of recognizing the full responsibility of physicians to their patients. This is now no longer possible, since in a decision of Lord Cooper in an action brought by a patient against the Edinburgh Royal Infirmary Board, he denied that the duty imposed by the National Health Act on hospital boards was a purely administrative one and said: "Under

the new Act and regulations the obligation on the State is in my view to treat the patient not merely to make arrangements for his treatment by and at the sole responsibility of independent contractors." *The Scottish Law Review* (August, 1955, page 177) argues that this does not threaten the relationship of physicians and patients. The hospital can no more give instructions to physicians about the care of patients than shipping companies can give orders to ships' captains about navigation. The *Lancet,* however, says that if the hospital is legally responsible for the physicians' actions and has to pay for his mistakes, sooner or later it will interfere with his clinical work in the hope of reducing these mistakes to a minimum. It is expected that the hospitals will introduce more and more rules limiting the physicians' freedom. In a referendum conducted by the Joint Consultants Committee (Scotland) among hospital physicians 10 to 1 were in favor of asking Parliament to reestablish in law their former relation to the management of the hospitals in which they work; i. e., the acceptance of full clinical and legal responsibility. It is clear that the medical profession in Britain is seeking to preserve in medicine the traditional ideal of service, which is only possible by full responsibility to the patient.

In the same issue of the *Lancet* a hospital physician states that it is now customary for some hospital management committees to issue books of rules for the medical staff. He was given a book of rules in which was stated: "(a) When a patient who has attempted to commit suicide is admitted, the house officer must notify the police immediately. (b) Resident officers shall give general anesthetics when required, but they shall not use chloroform or undertake spinal anesthesia." Presumably there would be no objection to their use of some new but potentially dangerous form of anesthesia. The voluntary reporting of patients to the police borders on unethical conduct. To frame rules of conduct for clinical practice in order to reduce the financial liability of the hospital in the event of litigation can only do harm to the profession and the public, and once it starts there is no knowing where it will stop.

Comparison of Iron Compounds.—Wilkinson and his co-workers have compared various iron compounds by therapy in patients with severe chromic anemia (*Lancet* **2**:482, 1955). They thought that trial in these patients would give more reliable results than in mildly anemic pregnant women, who are usually the subjects of trials of this sort. All patients had a hypochromic, microcytic iron-deficiency anemia, with a hemoglobin level of less than 12 gm. per 100 cc. and a mean corpuscular hemoglobin concentration of less than 30%. All patients were free from complications likely to interfere with hematopoiesis, and they were comparable as regards age, sex, and hemoglobin level. The duration of the test was 42 days unless the hemoglobin level reached 13.3 gm. per 100 cc. before this time. Ferric hydroxide, ferrous sulfate, ferric succinate, and ferrous gluconate were given three times a day in tablets containing a quantity of the preparation equivalent to 70 mg. of elemental iron. Gastric acidity was investigated, and patients who had achlorhydria were given diluted hydrochloric acid. Hemoglobin level, red blood cell count, color index, serum iron, and mean corpuscular hemoglobin concentration were estimated weekly. No other medicament was given. Ferric hydroxide in the dose given never produced more than a 4% rise in hemoglobin level during the 42 days. This was attributed to the low dose, the dose being normally given at 6 to 12 times this level. The ferrous sulfate, ferrous gluconate, and ferric succinate produced almost equal and satisfactory hematological responses. The daily increases in hemoglobin level were 1.22%, 1.12%, and 1.25% respectively. Of the patients, 13% were intolerant of ferrous sulfate (nausea and vomiting) and 4% were intolerant of ferric succinate and ferrous gluconate. A month's treatment with ferrous sulfate costs 35 cents, with ferrous gluconate $1.05, and with ferric succinate $1.61. The increased cost of the gluconate and succinate is only justified if the patient is intolerant of the sulfate.

Hospital Bureaucracy.—In a recent editorial the *British Medical Journal* (**2**:609, 1955) deprecates the extent of bureaucratic control in hospitals. It comments on the correspondence in the *Times* on hospital administration that arose out of the dismissal of a resident because he attended a medical conference without the consent of the hospital committee. Apparently his chief had no objection and was satisfied with the arrangements made for the care of the patients in his absence but the hospital administration thought differently and dismissed him. "The penalty for disobedience is instant dismissal, and that, for the administrator, is that. Whether the patients in the hospital from which the resident is dismissed suffer because of the discontinuity of treatment thus brought about, and because of the loss of this man's professional skill, appears to be of less importance than the correct execution of the administrative rule of law, almost military in its severity." The administrator looks on the hospital service as an inefficiently conducted industry, and if a physician working in the hospital service does not obey the regulations he is dismissed. Similar situations in industry have precipitated strikes. Although the physician has clinical responsibility, the hospital administrator has the power to interfere with his work, prevent his advancement, and injure his career. In another case a well-known specialist was "asked to agree to surrender a hospital ward to another specialty to save an official of the hospital board from personal embarrassment. . . ." For similar reasons the advice of professional appointment committees was overruled. In the *Times* correspondence there were complaints of a "tight hierarchical system" and of "the struggle that is being waged with increasing intensity between the administrators and the medical and nursing staffs of our hospitals." Some administrators appear to act as though administration were an end in itself and not a means to the care of the patient.

Blood Grouping Patients with Peptic Ulcers.—Clarke and his co-workers have investigated the distribution of ABO blood groups in 1,665 patients with duodenal and gastric ulcers (*Brit. M. J.* **2**:643, 1955). Compared with controls, they found a much higher frequency of group O blood among those with duodenal ulcers. The blood group distribution of patients with gastric ulcers was not significantly different from that of the controls. This finding of a significant difference in the frequency of group O in patients with duodenal and in those with gastric ulcers lends support to the view that they are two different conditions. Up to the present this view has been based on the differences in sex ratio, age incidence, precipitating factors, gastric acidity levels, and clinical course and the suggestion that these conditions are inherited independently. In carcinoma of the stomach in young diabetic patients and in pernicious anemia, there is a higher frequency of group A than in the controls. A common feature of these diseases is an abnormal level of gastric acidity, and it seems possible that the ABO genes may in some way modify the amount of hydrochloric acid a person can secrete.

Toxic Psychosis Due to Methyl Pentynol.—Methyl Pentynol is an unsaturated carbinol used in Great Britain as a sedative in place of barbiturates. Until recently it could be bought without a physician's prescription. Many undesirable side-effects have been attributed to it. Dr. F. Marley describes a 27-year-old woman in whom a toxic psychosis with neurological features due to Methyl Pentynol developed (*Lancet* **2**:535, 1955). She was admitted to the hospital suffering from rhythmic nystagmus, prominent ptosis of the eyelids, facial immobility, dysarthria, and diplopia. She was ataxic, had a positive Romberg sign, and her deep reflexes were elicited with difficulty. She had visual and aural hallucinations. On questioning she stated that she took 50 capsules of Methyl Pentynol in the two weeks prior to admission. She bought these without prescription or medical advice. Within four days of stopping therapy with the drug, her condition reverted to normal. She agreed to taking further quantities of Methyl Pentynol under supervision. A dose of 19 gm. three times a day caused a return of the condition observed on admission, and an electroencephalogram showed a marked abnormality in her frontal and central regions. Her condition became normal again shortly after therapy was stopped.

Rehabilitation of the Cardiac Patient.—Two years ago the British Council for Rehabilitation set up an expert working party to consider the facilities for cardiac patients, which included treatment and subsequent employment. The working party recommends that in the child unwarranted invalidism should be avoided and that where the presenting sign, such as a cardiac murmur, is innocent, this should be conveyed emphatically to

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physician, patient, and parent. It is proposed that health officers should keep a list of children in whom heart disease has been diagnosed or suspected by school physicians and that these children should be investigated by a cardiologist. If the physical signs are of no significance, all concerned should be informed. All patients should be followed up to make sure that advice has been acted on. Local general practitioners should be informed of the facilities and invited to refer children with actual or suspected heart disease. Alternative superannuation schemes should be devised for cardiac patients engaged in occupations where, at present, they are debarred from such benefits on account of their ailment.

Adenoidal-Pharyngeal-Conjunctival Viruses.—A group of viruses, the adenoidal-pharyngeal-conjunctival (APC) group, have been recovered from tissue cultures of a high proportion of surgically removed adenoids and tonsils. Dr. E. Zaiman and his co-workers have demonstrated the existence of these viruses in Britain and their association with disease (*Lancet* **2**:595, 1955). Adenoid tissue from 18 patients was cultured, and from the cultures 8 filtrable agents that were capable of causing degeneration in cultures of human embryo, lung epithelium, human kidney, and human embryo fibroblasts were obtained. Complement-fixing antibodies to the agents were demonstrated in the serums of 119 normal subjects at titers of 1:4 to 1:64. Titrations were also made on paired serums from 254 patients with acute respiratory disease of many types. Antibody levels in the serums in the acute phase were comparable to those in the above-mentioned groups. By complement fixation it was possible to recognize two cases of influenza A, 28 of influenza B, and 6 of influenza C infection.

International Pharmaceutical Federation.—At the 16th general assembly of the International Pharmaceutical Federation in London in September, the president of the British Pharmaceutical Society said that if pharmacy passed to the control of governments, however benevolent, there was grave danger that development would be hampered, professional enthusiasm hard to arouse, and the best interests of the public not served.

Meperidine Addiction.—The Ministry of Health has been asked by the World Health Organization to bring to the attention of physicians the risk of addiction to meperidine and the need for greater care in its prescribing. The expert committee states that addiction to this drug often results because of the widespread belief among physicians that it is less hazardous than morphine. Clinical and experimental experience shows that this is not so. As a potential agent of addiction, meperidine is no less dangerous than morphine, and this should always be borne in mind when prescribing the drug.

PERU

Endometrial Changes Induced by Hormones.—Dr. J. Arias Stella of the National University of San Marcos gave normal and castrated rats estrogen, chorionic hormone, or both in order to ascertain the individual and combined actions of these hormones on the endometrium. He found that an abnormal endometrial pattern characterized by unusual secretory activity, associated with extensive proliferative changes, can be elicited by the simultaneous action of estrogen and chorionic hormone. The nucleus of the proliferated epithelial cells is more vascular and swollen than normal. Most of these changes do not occur if the animals are given either estrogen or chorionic hormone alone but can be obtained when castrated rats are injected with large doses of estrogen and progesterone. Dr. Stella reported his findings at a special meeting held at the university in honor of Prof. Pedro Weiss, chief of the pathology department.

In normal rats receiving chorionic hormone and estrogen the ovaries were found to be greatly enlarged. Microscopic study showed the parenchyma to be entirely filled with corpus luteum and scattered follicles undergoing luteinization. The uterine walls were thicker than normal as a result of mucosal and muscular hypertrophy. In some segments of the endometrial surface showing atypical hyperplasia, there was a further marked proliferation with formation of cell aggregates that either invaded the stroma or bulged into the uterine lumen, adopting a papillary aspect. In these areas of proliferation as well as in some other portions of the mucosa, vacuolation and occasional mitoses were observed. Frequently, the vacuoles acquired a great size and by fusion formed large intraepithelial cysts. The glands were hyperplastic and showed scattered dilated lumens. In a second group of animals given only chorionic hormone, a normal progestational type of endometrium was obtained. Glandular hyperplasia was absent, and minimal vacuolation occurred in isolated cells of the epithelium. The author, by comparing the findings of the first group of animals with those of the second, concluded that vacuolation probably results from overproduction and faulty secretion of the hyperplastic cells. He therefore called them "intraepithelial retention cysts." In normal animals receiving estrogen alone the ovaries were smaller than normal and showed corpus luteum and follicles. On the other hand, frank endometrial hyperplasia and glandular cystic proliferation, with or without vacuolation, were observed in some areas of the endometrium.

The castrated animals receiving estrogen alone showed glandular hyperplasia with cystic formation. In another group of castrated rats given chorionic hormone alone the usual processes of secondary uterine involution followed castration, despite the administration of hormone. In castrated animals receiving both chorionic hormones and estrogen, no significant changes of the uterus were found and the histological pattern of the endometrium was similar to that observed during estrus. In the castrated animals receiving both estrogen and progesterone, gross and microscopic changes in the endometrium similar to those observed in the first group of normal animals were seen. These observations suggest that chorionic hormone stimulates the ovaries and releases large quantities of progesterone. Thus, it seems likely that the intensive vacuolation and proliferation result from the concurrent action of estrogen and progesterone, such changes being a synergistic effect of both hormones. On the contrary, the intraepithelial retention cysts occur rarely or not at all if estrogen or progesterone is given alone.

The cystic glandular hyperplasia induced by estrogen alone appears to be checked by the progesterone, since the normal animals given estrogen and chorionic hormone and the castrated animals given estrogen and progesterone did not show such changes. These observations support the idea, concerning the pathogenesis of the abnormal endometrial patterns found in certain cases of endometrial abortion, hydatiform mole, and chorioepithelioma, that the nuclear changes and the simultaneous occurrence of abnormal proliferative and secretory activities in some of these cases can be traced to hormonal actions. No matter what hormone was given, no squamous transformation of the epithelium was detected, but it is not known whether hormone administration over longer periods would ultimately lead to some form of metaplasia. The injections of hormones were given intramuscularly every day for 18 to 20 days.

Tuberculosis in Peru.—The Peruvian Tuberculosis Society held a symposium on the social, economic, and medical problems related to tuberculosis (*Revista del Viernes Medico,* vol. 3 and 4) in which it was stated that the insufficient funds available for the tuberculosis branch of the Ministry of Public Health and Social Welfare account in great part for the prevalence of tuberculosis in this country. Dr. Leopoldo Molinari said that the total morbidity rate for tuberculosis is 3% and the mortality rate is 2%, or 6.5 times that of the United States. At least 40,000 beds are needed for tuberculous patients, but the number available is only 3,000 (another 1,500 will be available soon). One of the main problems in the fight against tuberculosis is the need for financial assistance to needy patients. The Voluntary Antituberculosis Stamp authorized in 1947 has failed to provide the amount of money needed for this purpose. Dr. Cano Gironda said that the fight against tuberculosis aims at (1) the early detection of the disease by means of periodic mass roentgenographic examination, especially of persons who look healthy, in order to discover incipient lesions since adequate treatment of these patients with the new drugs gives a high proportion of cures; (2) establishing throughout the country a sufficient number of dispensaries, hospitals, and sanatoriums for the treatment of tuberculous patients;

and (3) providing financial aid to the patient's family. Dr. Huaco Vizcardo stated that more than 50% of the tuberculous patients in Peru lived in insanitary houses; in most of them a single room is shared with 3 or 4 other persons. In 60% of the homes of tuberculous patients, the family subsists on a grossly deficient diet due to a combination of poverty and ignorance. Dr. Pastor Balcazar reported that in the last decade in the "Dos de Mayo" Hospital of Lima for male patients, 16,172 tuberculous patients have been admitted. Of these, 5,236 have died; only 916 were cured; 7,079 were allowed to leave the hospital as improved but not cured; and the remaining 2,941 were discharged soon after admission as hopeless cases. Dr. Galvez stated that in Peru about 180,000 persons have tuberculosis (in Lima alone there are 30,000). About 12,000 patients die of this disease in a year. Many of these deaths were preventable. The highest incidence is among the natives who leave their homes far above sea level and come down to the lowlands to find work.

SWITZERLAND

Symposium on Poliomyelitis.—At the third symposium of the European Association Against Poliomyelitis in September, Professor Lepine of the virus division of the Pasteur Institute in Paris, France, stated that the amount of antibodies against poliomyelitis found in a person does not indicate the degree of immunity achieved. The antibody rate can give information on the general state of immunity of a population but tells nothing about the degree of individual resistance to paralytic infection. In virus diseases immunity resides especially in the tissues. Although the antibodies have a role in preventing viremia or in neutralizing the viruses that enter the blood stream, there is no proof that they alone intervene in the protection of the nervous system. Vaccination against poliomyelitis is directed against the paralytic complications of the infection rather than against the infection itself; therefore, reinfection through the digestive tract would not necessarily be prevented but might occur asymptomatically and act as a booster to the immunity produced by the vaccination. Because vaccination of an entire population would be wasteful of energy and money, and accidents might be caused in those few persons who cannot tolerate the injection of any foreign substance, it is recommended that only those persons who have been shown to have few, incomplete, or no antibodies be vaccinated. Determining these deficiencies is a tremendous job in itself, but it is the aim of public health authorities in France, Switzerland, and Italy, where the disease is relatively less common than it is in the Nordic countries. Lepine believes that vaccination should be performed in the latter half of the first year of life—that is, after the baby has lost the antibodies given to him through the placenta—but before his 12th month, since the greatest incidence of paralytic poliomyelitis occurs between the ages of one and three years. This first vaccination should be performed with a killed virus so as to obtain without risk the basic immunity needed for the appearance in the child's serum of the first antibodies against the three types of virus. To reinforce this primitive immunity, one could administer an attenuated vaccine, as advocated by Sabin.

Prof. Sven Gard of the virus division of the Stockholm Institute reported that vaccination campaigns have been undertaken in Sweden despite the reports of accidents occurring in the United States. No significant secondary reactions have been observed. It is theoretically impossible to obtain complete inactivation of the virus and preserve its antigenic power. The Swedish people are conscious of the risks of vaccination and are eliminating them gradually through research. They have already stopped using the Mahoney strain, which they consider too dangerous because of its instability. Campaigns have also been organized in Denmark this year, and more than 500,000 children were given subcutaneous injections, with no accidents reported. Preliminary results show that immunization against virus types 2 and 3 was successful, while that against type 1 was adequate in only 60% of cases, as Salk had predicted.

The acute phase of poliomyelitis is protean in character, and diagnosis outside of the paralytic phase is difficult. Professor Leroy of France advocates the use of anticoagulants and vasodilators such as tolazoline (Priscoline) every four hours to combat the aggravating vascular factor that produces anoxia and degeneration of the neurons in addition to the poliomyelitic lesions of the motor neurons. Dr. Charlotte Martin of Paris pointed out the importance of nursing and watchful care of patients with the acute phase of poliomyelitis, especially in the early paralytic stages in which recovery of function should be the primary goal. At this stage, pain must be combated and deformities avoided by proper positioning and hot packs. Dr. L. Schwartz of Brussels, Belgium, said that meningeal pain in the acute phase should be treated with aspirin and aminopyrine and peripheral pain should be treated with vasodilating agents. Professor Lassen of Copenhagen, Denmark, recommended caffeine for pain, whereas the German and French authorities preferred chlorpromazine.

Professor Dunois of Bern stated that deformities appear only as the result of muscular contractures of unknown cause. They occur in children and adolescents but not in persons who have attained full growth. Joint stiffness can appear after that age, but these are not deformities, strictly speaking. Paralytic deformities are observed only in the back and legs; the upper limbs are spared. This proves that not only the factor of movement is concerned here but also that of position. To prevent deformities, the therapeutic program must be varied according to the different phases of paralysis. The most important point is control of joint positions. Scoliosis can appear many years after paralysis has been forgotten. Dr. A. Grossiord of Garches, France, said that pain control is important in treating poliomyelitic rickets but position is also important. Maximal growth occurs where the pressure is least. A close watch should be kept for early evidences of muscular contractures. Improper nursing care of growing children with poliomyelitis can have tragic, irreversible consequences. If the patient is immobilized without the use of a corset, the sitting position is absolutely contraindicated. Instead, the inclined plane should be used, followed by standing and reeducation for walking. The child should circulate in the ward and go to class on a flat table with wheels. Kinetic therapy and hydrotherapy should be carried on as usual.

Dr. J. Knowelden of London, England, stated that immunizing injections against various diseases and tonsillectomy may predispose to poliomyelitis. His statistical evidence indicated that injections can either modify the distribution of paralyses in patients who would have had poliomyelitis anyway (paralysis of the arm in which the injection was given) or cause paralysis in patients who would only have had a nonparalytic infection. Tonsillectomy can favor a bulbar localization of the disease in certain patients, but its role is not entirely clear. Some authors have recommended that this operation not be performed in the late summer or early fall. Dr. R. C. Behrend of Hamburg-Eppendorf, Germany, admitted the predisposing influence of tonsillectomy, vaccination, the humoral state, and pregnancy but believed that other factors such as fatigue, participation in sports, climate, trauma, and surgical operations are much less important than some workers claim. On the other hand, Professor Mattia and Dr. Angela of Turin, Italy, consider fatigue an important aggravating factor in poliomyelitis. They based their position on experiments with monkeys. Others, using monkeys inoculated with poliomyelitis virus, studied the effect of lumbar puncture. In those monkeys that were late in developing symptoms, the easiest way of inducing symptoms was to perform a simple lumbar puncture, after which paralysis consistently appeared within 36 hours. This should not deter the medical profession from practicing lumbar puncture in all doubtful cases, because otherwise a diagnosis of tuberculous meningitis might be missed. On the other hand, in patients with known poliomyelitis lumbar puncture should, with rare exceptions, be deferred until the second week of illness.

Professor Lassen said that after the life-threatening acute phase is over and disorders of swallowing and circulatory complications are under control, the patient's chance of regaining independence from positive-pressure breathing apparatuses (combined with tracheotomy) depends chiefly on the severity and extension of paralysis of the muscles of respiration. From 70 to 80% of muscular regeneration occurs within the first three months. Withdrawal should be begun as soon as possible but must not be pushed, because fear might induce an intractable neurosis in the

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patient. Any patient treated with artificial respiration tends toward a state of hyperventilation that is accompanied by respiratory alkalosis. If this state is prolonged, it may play a part in the formation of renal calculi through prolonged secretion of an alkaline urine. This complication is often found in patients with chronic poliomyelitis. The stones are composed of calcium phosphates, poorly soluble in an alkaline milieu. The hardest point to get over in the process of withdrawal is sleeping without an apparatus. Respiratory infections must be avoided at any cost during this period. Once paralysis of swallowing is past, complications are checked, and a silver cannula has replaced the inflatable cuff, it is then permissible to consider replacing the positive-pressure apparatus by a cuirass-type or rocking-bed respirator. The cannula may be removed when the patient can breathe properly with the cannula blocked. In the last five months of 1952, Professor Lassen's department received about 3,000 patients with a diagnosis of poliomyelitis that was confirmed in 2,300 cases. Of a total of 1,250 patients with paralysis, 333 had signs of respiratory insufficiency. Seventy per cent of the 139 deaths occurred during the first week in hospital, but only 5% occurred after the first month of illness. Respiratory paralysis usually progresses rapidly. In most patients it lasts only a few days. The combination of paralysis of the diaphragm and of the intercostal muscles is the most dangerous and often leads to a chronic state, while the patients who have only one or the other regain respiratory function before the first month is up.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACT

Malpractice: Surgeon's Liability for Acts of Anesthesiologist.—The plaintiff sued a surgeon and an anesthetist for injuries arising from the administration of a spinal anesthetic. From a judgment in favor of the plaintiff, both defendants appealed to the Supreme Court of Oklahoma.

The plaintiff was referred to the defendant surgeon for removal of a chronic appendix, which had been bothering her for some time. He told her that an anesthesiologist, whom she did not know, would administer the anesthetic. The plaintiff insisted that a general anesthetic, not a spinal, be given, and the surgeon agreed to that. The plaintiff was admitted to the hospital and on the day before the operation was assured by an assistant to the defendant surgeon that she would be given a general anesthetic. On the following morning, before being taken to the operating room, the plaintiff was given an injection of morphine, which left her somewhat hazy and groggy. She was placed on the operating table. Present in the operating room at that time were a nurse and the defendant anesthesiologist. The defendant physician was not there and did not come into the room while she was conscious. The nurse told her to turn on her right side. She said that she had never before had any type of operation nor had she ever been in an operating room, so that she knew nothing of the procedure of an operating room nor of how anesthetics were given. She therefore obeyed the orders of the nurse and turned on her right side. The nurse placed one hand beneath her knees and the other at the back of her neck and pulled her into a bowed position. The plaintiff felt a sting in her spine and then a grating sensation, and pains traveled down her thighs, legs, and feet. She heard the defendant anesthesiologist say to the nurse, "That must be just in the side," and immediately after he said this the nurse gave her an injection in her right arm and she went to sleep. When she awoke she was back in her hospital room. She had semiconscious periods but did not become fully conscious until three days later; from that time on she has had heavy cutting pains in her body from the hips down and has not been able to move any part of her body from the belt line down.

On behalf of the plaintiff an expert witness testified that the needle used in injecting the spinal block had punctured the spinal cord, allowing leakage of the spinal fluid. This resulted in inflammation of the spinal cord causing partial paralysis from the waist down, ankylosis of the hip joints, complete loss of power in the feet, shrinking of the legs, and migraine headaches. On the other hand, witnesses for the defendants testified that the plaintiff was suffering from poliomyelitis and that her paralytic condition was in no way related to the spinal injection. The anesthesiologist testified that before giving the injection he had checked the plaintiff's chart and had noticed nothing thereon that would indicate that a spinal block would be dangerous. He admitted that the plaintiff had told him that she did not want such an anesthetic, but he said that he assured her that it would be perfectly safe. She responded as follows, "Well, I will not be obstinate, but I want to go to sleep."

On appeal the Supreme Court first held that the evidence as to the cause of the plaintiff's condition was such that a jury would be justified in finding that the spinal injection was the causal factor. There was no evidence of any negligence, however, so the theory of the plaintiff's suit was one of assault and battery—in other words, giving a spinal anesthetic without the consent of the patient. On this theory the Court pointed out that from the state of the evidence the jury could find that the anesthesiologist well knew that the plaintiff objected to a spinal anesthetic but that he gave one anyway. Under the law this constitutes a battery, and the defendant anesthesiologist is liable for the harmful consequences of such an unlawful act. As to the defendant surgeon, however, the Court held that there was no evidence showing that he had consented to the spinal anesthetic or that he had failed to do anything that he could have reasonably been expected to do. He put the plaintiff's request on the chart for the anesthetist to read, and the anesthetist did read it.

Accordingly, the Supreme Court affirmed the judgment against the defendant anesthesiologist but reversed the judgment against the defendant surgeon. *Woodson v. Huey, 261 P. (2d) 199 (Okla., 1953).*

MISCELLANY

THE HISTORY OF SOCIAL SECURITY

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Perhaps I should preface my remarks by saying that the general heading, "History of the Social Security Act," is rather broad and could consume much more space than can be allotted. To attempt to give the subject its complete treatment, I would be forced to go back at least as far as the early 19th century and try to trace the evolution of the social theories of the economists of the European school. However, I think we will bypass the theories of the Utopian socialists, the Marxian socialists, and others and skip the social security experiments in Germany under Bismarck. I am reasonably certain that most are familiar with the trends in the United Kingdom that began to develop in 1911. The social security program came along somewhat later in France and was not adopted until 1928.

We are concerned with what happened in the United States during the depths of the great depression in the 1930's. It was then that the United States brought the social security system into being. The American people always have believed in individual initiative—in depending on their own ingenuity and in the philosophy that hard work will bring rewards. There was an incentive to work and to save and to succeed. Naturally, the depression hit hard. It wiped out savings and even denied men the opportunity of finding jobs.

Thus, the Social Security Act of 1935 was born of the depression in a climate that was receptive to government assistance toward the solution of problems resulting from a period of economic distress. By 1935 the American people had become conditioned to federal guarantees in other fields that at the time seemed logical and necessary. It was but a step to a broader

concept that resulted in a nationally administered compulsory system of old age insurance, a system of unemployment insurance that would be operated by the states under federally prescribed standards and with federal aid, and a system of federal grants to the states intended to apply to other types of aid to the needy.

Government social insurance was designed on a two-pronged approach. As set up, it required that by individual thrift the beneficiary make regular contributions toward the cost of benefits to be received on retirement. On the other hand, the government through partial assistance for social welfare accepted the responsibility of providing for the handling of emergencies that cannot be coped with by private effort.

It is important to bear in mind that in the term "insurance" as it is freely used in connection with the Social Security Act and Old-Age and Survivors Insurance benefits, there is little resemblance to the term "insurance" as used in coverage provided by private companies. "Social insurance" does contain an element of private insurance practice in that in both cases premiums are paid. However, the resemblance ends there. Where the welfare factor enters in, there can be no actuarial relation between premiums paid in and benefits paid out as there is in private insurance.

A revealing view of social security can be obtained from a summary of the history of the Social Security Act from its inception to the present time. By reviewing events chronologically, I think the extent of the growth and expansion of the system and its benefits will be apparent.

The Social Security Act officially became law Aug. 14, 1935. The Social Security Board was set up Aug. 23, 1935.

On Aug. 10, 1939, the Social Security Act was amended to provide OASI benefits for dependents and survivors. This amendment made the tax applicable only to the first $3,000 in wages.

In January, 1940, monthly benefits were first payable under OASI.

On Jan. 1, 1950, OASI contribution rates were increased to 1.5% each for employers and employees.

In October, 1950, the first payments were made under the federal-state program of aid to the permanently and totally disabled.

In February, 1951, the number of aged persons receiving OASI benefits for the first time became greater than the number of recipients of Old Age Assistance aid.

On July 18, 1952, the Social Security Act was amended to increase benefits under OASI.

On April 11, 1953, reorganization plan no. 1 abolished the Federal Security Agency and transferred all its powers and functions to the Department of Health, Education, and Welfare.

On Jan. 1, 1954, OASI contribution rates were increased to 2% each for employers and employees.

On Aug. 3, 1954, the Vocational Rehabilitation Act was amended to call for the cooperation of vocational rehabilitation agencies with state public assistance agencies, the bureau of OASI, and other public agencies providing service related to vocational rehabilitation.

On Sept. 1, 1954, the Social Security Act was amended to extend OASI coverage to farmers, self-employed members of specified professions, additional farm and domestic employees on a voluntary group basis, to members of state and local government retirement systems, and, at the election of the individual, to ministers and members of religious orders. The act was also amended to raise to $4,200 the wage basis for tax and benefit computation purposes, raise ultimate contribution rates, increase benefits, liberalize the retirement test, and protect benefit rights of disabled persons through a disability freeze provision.

The Social Security Act was amended by the addition of New Title XV to provide unemployment insurance benefits for federal civilian employees financed by federal funds and paid by state agencies. The federal unemployment tax act was amended to include firms employing four or more persons in 20 weeks after Jan. 1, 1956.

By February, 1955, OASI beneficiaries numbered seven million.

Within 20 years the Social Security Act has been amended as follows with changes in the minimum and maximum OASI benefits payable:

Year	Minimum, $	Maximum, $
1935.....	10	85
1950.....	20	80
1952.....	25	85
1954.....	30	108

The system's rate of growth has been hinged to population gain as well as to the inclusion of additional groups in its coverage. In 1935 the United States total population was 128 million. In 1935 the total civilian labor force was 52,230,000. In 1954 the total population was 164 million and the total civilian labor force, 64,468,000. To date, major amendments to the Social Security Act in 1950 and 1954 have resulted in the extension of OASI coverage to 9 out of 10 of the nation's labor force. Within this 20-year period the system has grown to the point that 69 million workers will be in covered jobs this year, about 7.5 million beneficiaries are receiving checks totaling 385 million dollars each month, and, as of this year, about 90% of all paid jobs are covered under OASI.

Of course, the expansion of the system is reflected in the tax base increase. In 1937 the level was $3,000. In 1954 it climbed to $4,200. The rate of taxation has brought about periodic increases. In 1937 the tax was 1% of the payroll for employee and employer; in 1950, 1.5%; and in 1954, 2%. In 1956, if pending legislation becomes law, it will increase to 2.5%. The 1954 amendment set an ultimate maximum of 4% each for employee and employer. However, pending legislation would elevate that figure to 4.5%.

We all recognize that statistics are flat and colorless, whether they pertain to human beings or to dollars and cents. We have to explore beneath the surface figures to interpret them properly. Take, for instance, the statement that 9 out of 10 workers are covered under OASI. This means that they will receive monthly retirement benefits at age 65—and their widows and orphans may get monthly payments upon the death of the breadwinner.

Spokesmen for the Department of Health, Education, and Welfare emphasize that the administrative cost of operating the social security system has been held to minimum levels. However, it is all too clear that, with our expanding population and with 90% of the labor force given blanket coverage under the act, the growth of the system has far exceeded expectations of its early planners. It is significant to note that there are 14 million men and women in the United States now aged 65 or over and that nearly 60% of this group are receiving Old-Age and Survivors Insurance benefits or are working under the system and have acquired or are acquiring protection.

From the facts available, it is obvious that a system designed to provide social insurance as the first line of defense against economic insecurity has grown at an almost unbelievable and perhaps unmanageable rate of speed. As we reflect on this unchecked growth and the ever-broadening coverage and ever-increasing benefits, let us remember that this is 1955. If the same rate of growth and expansion occurs in the coming years at the same rate of speed, who could predict the outcome?

Spokesmen for the Department of Health, Education, and Welfare have emphasized that the department is constantly studying the programs to meet additional needs as they develop. Consider this statement in line with the prediction by HEW that the recent extensions of coverage in OASI alone will be providing lifelong benefits for nearly three-fifths of those persons aged 65 or over in the United States within 10 years.

The philosophy of the career executives in the social security system is to provide ever-increasing coverage, even universal coverage, and, with increased benefits, eventually perhaps 100% of the working population will be covered. HEW states that since social security is not a static program, it is evident that the intents, purposes, and aims of the social security system are to encourage the growth, expansion, and all-inclusive coverage of that particular branch of government. This, indeed, is sufficient to cause anyone to reflect soberly on the future for social security coverage in this country.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Use of Radioactive Iodine in Diagnosis and Treatment of Hyperthyroidism: Ten Years' Experience. F. M. Chapman and F. Maloof. Medicine **34**:261-321 (Sept.) 1955 [Baltimore].

This review presents observations gained from the treatment of patients with radioactive iodine during the period from 1943 to 1953. Radioactive iodine is an effective form of therapy for patients with hyperthyroidism. The use of the isotopes I^{130} and I^{131} is based upon the natural avidity that the thyroid has for iodine and the emission of beta rays that radiate a distance of a few millimeters to produce an effect primarily in thyroid tissue. The uptake of radioactive iodine by the thyroid, the serum-protein bound iodine and the basal metabolic rate are the most informative tests in the evaluation of thyroid function and in the diagnosis of hyperthyroidism. In patients with hyperthyroidism, the response to oral doses of radioactive iodine is manifested by a gradual return of the metabolic processes toward normal. Most patients become euthyroid in two months. Some respond gradually over a period of 12 months or longer. When myxedema occurs, it is usually evident in four months, but it has been observed to develop as long as eight years after treatment. Because of this late appearance, the incidence of myxedema may increase with time. Seventy-five per cent of 520 patients treated with I^{131} responded to a single dose, 12% required more than one dose to achieve normal thyroid function, and 8% became myxedematous. The remaining 5% manifested a variety of clinical reactions. The authors not only doubt the value of using antithyroid drugs after radioactive iodine therapy but even feel that their use might be contraindicated. There has been no true recurrence of hyperthyroidism after the use of radioactive iodine for diffuse hyperplasia of the thyroid. Although more time will be required for the exact evaluation of the recurrence rate, the authors believe that it will be lower than after operative treatment, in view of the biological effects of this radiation on the thyroid cells. As regards the selection of patients, the policy has been to avoid treatment in persons under 40 years of age, because of the fear of inducing a cancer of the thyroid. Thyroid tissue removed from patients up to 12 years after treatment with I^{130} and I^{131} shows variable degrees of irregularity of the nuclei, persistent hypertrophy of acinar cells, and fibrosis. As time has passed and no cancer of the thyroid attributable to radioactive iodine has been demonstrated, the fear of it is diminishing. The authors do not advise the use of radioactive iodine in pregnant women beyond the fourth month of gestation. Although patients who have nodular goiters and hyperthyroidism can be effectively treated with radioactive iodine, it is felt that they are best treated by subtotal thyroidectomy, because of the possibility that one of the nodes may be malignant. An intense form of hyperthyroidism is indicated by severe ocular signs and symptoms. In 4 of 44 such patients, the eyes became worse after treatment with radioactive iodine. It was impossible, however, to ascribe this clinical course to the use of the isotope. Patients with hyperthyroidism and severe heart disease usually respond favorably to radioactive iodine. Myxedema imposes an added burden on the heart, and so relative hypothyroidism is a more desirable state for patients with heart disease. Swelling of the submaxillary glands, aching of the teeth, and loss of hair are minor biological effects of radioactive iodine therapy. Indexes of thyroid function after I^{131} therapy show a close correlation with the clinical evaluation in the majority of patients.

Some Cases of Coronary Localization of Thromboangiitis Obliterans (Bürger's Disease). P. Capra Marzani and F. Barberis. Riforma med. **69**:715-719 (June 25) 1955 (In Italian) [Naples, Italy].

Thromboangiitis obliterans (Buerger's disease) in the coronary artery was observed recently by the authors in four men, heavy cigarette smokers, under or about 50 years of age. The symptoms of these patients; their age; the absence of heart disturbances, valvular defects, aortic lesions, arterial hypertension, and syphilitic, diabetic, and tuberculous manifestations; and the laboratory findings confirmed the fact that thromboangiitis obliterans was definitely present in the four men. In the differential diagnosis, arteriosclerosis obliterans, Raynaud's disease, and thrombophlebitis were ruled out. In the first and second patients the coronary symptoms appeared suddenly and preceded by several months and several years, respectively, the peripheral symptoms. In the second, a gastric ulcer followed the infarct and preceded the vascular disturbances. The fourth patient presented with a myocardial infarct that simulated an acute abdominal condition. Such infarcts, according to some authors, occur during digestion. Despite this limited number of cases, the authors' experience points to the possibility that severe coronary lesions and peripheral vascular alterations may have the same causative factor. It is suggested that patients with vascular disease, especially those with initial and mild peripheral signs, be subjected to systematic and periodical electrocardiographic examinations so that prophylactic and therapeutic measures may be taken.

Pulmonary Tuberculosis Due to Bacilli Resistant to Streptomycin and Isoniazid. J. McC. Murdoch and I. W. B. Grant. Lancet **2**:587-588 (Sept. 17) 1955 [London, England].

The man whose history is reported was first seen as a contact of his sister, who had pulmonary tuberculosis. At that time, when he was 20 years old, roentgenograms of his chest gave no indication of tuberculosis. He subsequently served in the navy and was not seen again until five years later, when roentgenologic examination showed enlargement of the right hilar shadow and disease in the right lower lobe. The Mantoux reaction was strongly positive. A provisional diagnosis of active pulmonary tuberculosis was made, and treatment with aminosalicylic acid and with isoniazid was started. Positive sputum cultures obtained from the pretreatment specimens were subsequently tested for bacterial resistance to streptomycin, aminosalicylic acid, and isoniazid, and the organisms were found to be resistant to streptomycin and isoniazid, but sensitive to aminosalicylic acid. Subsequent sputum specimens always showed the tubercle bacilli to be resistant to streptomycin and isoniazid. As the patient's sister, with whom he had been in close contact, was excreting tubercle bacilli resistant to streptomycin and isoniazid and as the organisms isolated from the two patients showed an almost identical pattern of drug resistance, it seems reasonable to assume that the man was infected by his sister. So far as the authors know, this is the first instance of infection by isoniazid-resistant bacilli in which the source of infection could be traced. The patient's sputum became negative after he had been treated for a number of weeks with viomycin and oxytetracycline. The chest films also became normal, and he was able to resume his occupation. The organisms isolated from the patient's sputum were of low virulence for a guinea pig. In view of his rapid response to what has been described as a less effective treatment, that is, viomycin and oxytetracycline, it is possible that the bacilli were also of low virulence for the patient; but the fact remains that they were initially capable of producing a frank pulmonary lesion. The clinical significance of in vitro isoniazid resistance

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The place of publication of the periodicals appears in brackets preceding each abstract.

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has been denied by some, who continue to use isoniazid by itself in pulmonary tuberculosis. The fact that the reported case supports the opposite view is considered as additional justification for reporting it.

Differential Diagnosis Between Benign Ulcer and Ulcerating Carcinoma of Stomach. B. Sepúlveda, J. Deschamps, G. Serrano and M. Quijano. Rev. invest. clín. **7:**127-142 (April-June) 1955 (In Spanish) [Mexico, D. F., Mexico].

Two hundred thirty patients with peptic ulcer were observed during the last five years at the Hospital de Enfermedades de la Nutrición of Mexico City. Ulcerating carcinoma was detected in 21 patients by histological study of tissue removed during gastroscopy. The clinical symptoms and roentgen signs of these diseases are so similar that a differential diagnosis is difficult. A presumptive diagnosis is made by correlating the roentgen and gastroscopic signs. Ulcerating carcinoma shows during endoscopy as a lesion of dark red color with irregular borders, a pale ulcerated mucosa, and rigid infiltrated margins. A positive diagnosis can be made only by a histological study of a fragment of the borders of the ulcer taken during gastroscopy or by the lack of response of lesions to medical treatment. The program followed in the Hospital de la Nutrición is as follows: 1. If the roentgen and gastroscopic signs are those of ulcerating carcinoma, immediate operation follows. 2. If the same signs are those of benign ulcer, strict medical treatment is given for four weeks, at the end of which the roentgen examination and gastroscopy are repeated. If the roentgen and gastroscopic signs of malignancy persist, a diagnosis of probable ulcerating carcinoma is made and an immediate operation performed. If signs of malignancy disappear, medical treatment is continued for two years. During the first year, the patient is seen in consultation every month. Roentgen examinations are made every three months. During the second year, the patient is seen in consultation every three months. Roentgen examinations are made every six months. If the ulcer reappears months or years after having completely healed, it indicates malignancy. Immediate operation follows.

Laparoscopy in Clinical Practice: Importance of Controlled Hepatic Biopsy. G. Sotgiu and G. Lenzi. Minerva gastroenterol. **1:**2-12 (June) 1955 (In Italian) [Turin, Italy].

Although laparoscopy is a valuable and often a decisive diagnostic means, it is not widely used in Italy. The main objection to this procedure, especially by surgeons who overlook the fact that patients do submit to it much more easily than to a laparotomy, is that the abdominal organs are best studied by means of the latter method. Laparoscopy is indicated for conditions involving the peritoneum, the liver, and the biliary tracts. It should always be performed by an experienced person under conditions of perfect asepsis and antisepsis. At the authors' clinic laparoscopy is always preceded by induction of a pneumoperitoneum performed with an instrument that makes it possible to measure the exact amount of air introduced and the pressure of the air within the abdominal cavity and to keep automatically, for the entire period of the laparoscopy, the desired pressure therein independently of the movements of respiration and of abrupt contractions of the abdominal walls. After the laparoscopy is completed, the air is removed through the opening into which the laparoscope was introduced; the small opening is closed; and healing takes place rapidly. The authors performed 102 laparoscopies on patients with diseases of the liver, biliary tracts, and peritoneum. Their good results proved that it is possible with this procedure to solve diagnostic doubts, confirm a tentative diagnosis, establish a diagnosis that would not have been possible with clinical investigations alone, and select the best medical or surgical treatment. A procedure closely linked to laparoscopy is controlled or laparoscopic liver biopsy, with which the accidents that are due to the standard blind method of liver biopsy are avoided. The authors state that liver biopsy should always, except in very rare instances, be performed under laparoscopic control. Laparoscopy alone or combined with controlled liver biopsy enabled them to solve with certainty a differential diagnosis between specific and cancerous peritonitis; catarrhal jaundice with typical and atypical course and neoplastic jaundice; and severe hepatitis, abscesses, and neoplasms of the liver. It also enabled them to identify hepatic amyloid degeneration and echinococcosis of the liver; to establish, together with the histological study of the biopsy specimen, the exact phase of hepatic and cirrhotic processes; and to determine whether a condition was operable.

Esophageal Varices: Causes Other Than Cirrhosis and Portal Vein Block. E. D. Palmer and I. B. Brick. J. Am. Geriatrics Soc. **3:**681-686 (Sept.) 1955 [Baltimore].

Palmer and Brick are concerned with the esophagoscopic detection of varices, being convinced that, in cases of upper gastrointestinal hemorrhage, it is necessary to consider the possibility of esophageal varices as the cause, even though there is nothing to suggest the presence of cirrhosis or portal vein block. Patients were studied esophagoscopically, as the clinical situation dictated, during the course of their regular evaluation or treatment. Thus the data were collected at random, there being no routine survey of various diseases. Except for the pregnant women and 30 of the achalasia patients, persons were included in this compilation only if the liver had been studied histologically, either by needle biopsy or at autopsy. All patients with the diagnosis of schistosomiasis, extrahepatic portal vein block, or cirrhosis, including hemochromatosis, were excluded. Examination for esophageal varices was made under 4-diameter magnification with the Eder-Hufford esophagoscope. Gastroscopic examination for gastric varices was made in 69 patients, but there was only one positive result. The criteria for inclusion were met by 166 patients, classified in 1 of 12 disease categories. Varices were found in 61, but in some of these they were of minimal diameter and extent. It was demonstrated that esophageal varices occur in many clinical situations not heretofore suspected of being accompanied by portal hypertension. Several types of liver disease other than cirrhosis can produce varices. These lesions may develop quickly. Examination of 21 patients during the active phase of infectious hepatitis, for instance, showed esophageal varices in 11, in some as early as six days after onset of the disease. The varices were judged to be mild in nine of these patients, and all of them were too small to permit satisfactory measurement of portal pressure. It was also found that chronic congestive heart failure and the latter half of pregnancy are particularly likely to give rise to esophageal varices, although they rarely cause hemorrhages in these conditions.

Oral Treatment of Pernicious Anemia with Vitamin B_{12} Without Intrinsic Factor. E. H. Reisner Jr., L. Weiner, M. T. Schittone and E. A. Henck. New England J. Med. **253:**502-506 (Sept. 22) 1955 [Boston].

Of 43 patients with pernicious anemia, 13 were given 1 mg. of vitamin B_{12} orally in tablet form once a week, 3 received the same dose by the same route twice weekly, 21 every second week, 3 every third week, and 3 every fourth week. If there appeared to be any hematological or neurological relapse, the interval between doses was diminished by half. In none of the patients was intrinsic factor added to the vitamin B_{12}. The patients were followed on this therapy for periods of 12 to 28 months, with an average of 20.9 months. From studies on relapse rates with the different dosage schedules it appeared that, with a few possible individual exceptions, weekly treatment with 1 mg. of vitamin B_{12} would be satisfactory for all patients with pernicious anemia.

A Comparison of Cortisone and Aspirin in the Treatment of Early Cases of Rheumatoid Arthritis: A Second Report by the Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, A. C. T. H., and Other Therapeutic Measures in Chronic Rheumatic Diseases. H. Cohen, E. G. L. Bywaters, W. S. C. Copeman and others. Brit. M. J. **2:**695-700 (Sept. 17) 1955 [London, England].

Of 61 adult patients with early and uncomplicated rheumatoid arthritis, 30 were treated with cortisone and 31 with acetylsalicylic acid (aspirin), their allocation to treatment with one or the other agent being made entirely at random. Observations

of these two groups of patients in the course of the first year after the start of the treatment were reported previously (*J. A. M. A.* **156:**289 [Sept. 18] 1954) and showed that the patients had run a closely parallel course in nearly all respects, including joint tenderness, strength of grip, tests of dexterity of hand or foot, and clinical assessments of the activity of the disease and of the patient's functional capacity. In the present report the comparison of the two treatment groups was extended to approximately two years from the beginning of the treatment. In the second year of therapy, treatment with one or the other agent was continuous and individualized by the physician in charge to meet each patient's need. The average value of the maintenance doses employed was 80 mg. of cortisone daily and 4.5 gm. of aspirin daily. At approximately the end of two years of treatment, 58 of the original 61 patients were reassessed clinically, submitted to some simple objective tests, had roentgenograms made of their hands and feet, and had their hemoglobin levels and erythrocyte sedimentation rates measured. In no respect did the two groups differ by more than might easily be due to chance and in most respects they were distinguished more by their similarities than by their differences. At the end of two years, therefore, as previously reported at the end of one year, it appears that for practical purposes there has been remarkably little to choose between the use of cortisone and aspirin in the management of these patients.

Low Back Pain: The Hyperextension Syndrome. I. Macnab. Canad. M. A. J. **73:**448-454 (Sept. 15) 1955 [Toronto, Canada].

One common type of low back pain is brought on by hyperextension of part or of all of the lumbar spine. It is commonly seen during and following pregnancy and in the 35 to 45 year age group, in people of increasing weight and decreasing tone of abdominal muscles. The patient complains of pain over the lumbosacral region. The pain may be referred to both buttocks and on occasions may be referred down the back of the thigh, but is not experienced in the calf. Pain radiating down the back of the leg as far as the calf is much more likely to be due to nerve root irritation. In the hyperextension syndrome, the pain is aggravated by any activity that puts an extension strain on the back, such as lifting the baby out of the play pen, pushing up windows, or prolonged stooping as in bedmaking or washing the hair over a basin. During the acute severe attack of pain the patient should be nursed in bed in a flexed position (semi-Fowler). This is achieved by putting a small wooden crate under the mattress at the foot of the bed and a rolled-up blanket or another box under the mattress at the head of the bed. The buttocks should rest on the part of the mattress that is beginning to slope up towards the raised lower end of the bed. When the pain has subsided the patient should be given exercises designed to build up the strength of the gluteal and abdominal muscles in an attempt to decrease the lumbar curve. One of the most important aspects of treatment is reeducation. The patient should learn to stand with the stomach pulled in and the lumbar spine straight. The most comfortable way for these patients to sit is with the knees higher than the hips—as when the feet are placed on a footstool or as when sitting with the knees crossed. Housewives must be told that all their cleaning equipment should have long handles and that they must not stoop forward when using it. They must not carry heavy loads in the laundry basket. If they stand for any length of time, they should keep one foot on a low footstool. The kitchen should be so arranged that articles in daily use are stored on shelves at shoulder level. Some patients require a back support in addition, and this should be so designed that it tends to flatten the lumbar spine. Corsets for women should be reinforced with four rigid posterior steels, which should not curve to fit the spine but should run in a straight line from the thorax to the sacrum, so that when the front of the corset is tightened up the spine will be flattened against the steels. If this point is not observed, the corset will tend to hold the spine in the position of deformity and perpetuate the symptoms. For men, the Williams flexion brace is ideal. These patients should avoid heavy lifting, reaching, and stooping. They should not get overtired. The obese must lose weight; it is almost impossible to stop back pain in a patient who is overweight and who has a hyperextended spine.

Micrococcus (Staphylococcus) Enteritis After Antibiotic Treatment with Special Regard to Fatal Cases. E. H. Thaysen, K. R. Eriksen, K. Fischermann and H. E. Knudsen. Ugesk. læger **117:** 1047-1054 (Aug. 18) 1955 (In Danish) [Copenhagen, Denmark].

Antibiotic agents, particularly Aureomycin and Terramycin, with potent effect on the intestinal flora can introduce risk of the development of Micrococcus (Staphylococcus) enteritis. Reduction of intestinal flora through antibiotic treatment allows multiplication of micrococci in the intestinal tract. Fatal Micrococcus enteritis is relatively rare, although a number of cases have undoubtedly escaped publication and/or diagnosis. Five fatal cases from Copenhagen during the last year are reported. It is impossible to foretell which patients may be liable to the complication. It is manifested by severe diarrhea, with green, watery stools, and by toxemia, dehydration, and circulatory collapse. The first symptom generally appears from the third to the fifth day of antibiotic treatment. In the gravest cases the shock is refractory to treatment and leads to death in from one to six days. The use of Aureomycin and Terramycin can be continued, provided the indications are clear and the patients are carefully controlled during treatment. Grave Micrococcus enteritis has been observed only in hospital patients. Peroral administration of the two tetracycline derivatives is believed to be more risky than parenteral administration. During treatment with tetracyclines, laxatives and enemas should probably not be given. Dyspepsia with anorexia, vomiting, and possibly milder diarrhea calls for especially careful control. If the symptoms are accentuated and if fever occurs, the treatment should be terminated at once. If there is marked diarrhea or unexplained circulatory collapse, immediate peroral administration of erythromycin (300 to 400 mg. four times daily) is advised. Before treatment with erythromycin, cultivation from the feces on a special medium with reference to micrococci is necessary, together with determination of resistance as a guide for continued treatment. If the micrococci prove resistant to erythromycin, Nebacetin can be tried.

Clinical-Immunobiological Observations in an Epidemic of Ornithosis, with Particular Consideration of the Effect of Chlortetracycline (Aureomycin). W. Benstz. Medizinische, no. 35, pp. 1186-1189 (Aug. 27) 1955 (In German) [Stuttgart, Germany].

Of 11 patients between the ages of 4 and 64 years with ornithosis who were admitted to the first medical clinic of the City Hospital of Karlsruhe, Germany, in the fall of 1953, 8 had been infected by parakeets and canaries bought from the same animal wholesale dealer in the city, and 3 had been infected by parakeets bought from two animal retail dealers in the suburbs. The author prefers the term ornithosis to psittacosis, because homebred birds such as sparrows, pigeons, finches, chickens, ducks, and pheasants may be the carriers of the virus as well as the exotic birds. Of the 11 patients, 6 (group 2) were treated with chlortetracycline and 5 (group 1) were not treated with this antibiotic. The daily dose of chlortetracycline varied from 1 to 2 gm., which was given in divided doses in the course of 24 hours. The total dose was 6 and 10 gm., respectively, in the two patients who received a daily dose of 2 gm., and the total dose varied from 11 to 24 gm. in the four patients who were given a daily dose of 1 gm. Temperature was restored to normal within 12 to 48 hours. The pulse rate also dropped, but its fall was more or less delayed depending on the severity of the disease. In the five patients of group 1, the titer of the complement fixation reaction was more or less increased eight weeks after the temperature was restored to normal, and in two of these it was still increased after 12 months. In group 2, which consisted of severely ill patients whose titers were higher on the average than those of the patients in group 1, the titer rose in two after the temperature was restored to normal. After 12 months, the complement fixation test gave a negative result in two, two others showed a marked drop of their titers, and the remaining two still had increased titers. Because of the small number of patients and the heterogenic results, changes in the titer resulting from chlortetracycline therapy can not be considered a definite sign of relief of the reticuloendothelial system. Shift to the left in the differential blood count, leukocytosis, and erythrocyte sedimentation rate were restored to normal within

40 to 60 days in group 2, and convalescence was particularly delayed in two patients as compared to the serologic findings. The relatively long-continued duration of an increased titer also after chlortetracycline therapy, corresponding with circulatory lability and generally reduced work capacity, suggests that antigens may be present in the organism for a long time after temperature has been restored to normal; additional therapeutic measures may, therefore, be required. Prolonged treatment with chlortetracycline seems to be preferable to that with higher doses for a shorter period. Treatment should be continued until the titer shows a tendency to fall, i. e., until the defense powers of the body do no longer require exogenous support. This may be obtained with a total dose of 15 to 25 gm. of Aureomycin given in the course of 15 to 25 days.

Practical Value of Determinations of Resistance to Antibacterial Agents. E. Steen. Nord. med. **54:**1269-1273 (Aug. 18) 1955 (In Norwegian) [Stockholm, Sweden].

Carefully performed determination of resistance is a valuable aid in the selection of the most effective therapy. It is not an absolute guide, as the tests do not take into account the conditions in vivo. The clinician has to consider the interplay between the bacteria and the organism, the localization and course of the infection, and toxic reactions, possible allergy, and ways of administration and dosage. This may lead to the choice of not the agent most effective in vitro but perhaps the next most effective. If the causative bacteria show wide variation in sensitivity, as micrococci (staphylococci), enterococci, and some gram-negative bacteria, it is important to isolate the bacteria and determine the resistance. If need be, treatment with the chemotherapeutic agent considered the most suitable can be started as soon as the test is made. If the treatment is without effect in the course of two or three days, it must be revised; by this time the answer to the resistance test should be available. Determinations of resistance should be carried out in the case of fulminant infections or of relapse during treatment. In chronic infections, where the time factor does not play an important part, and when toxic or allergic reactions exclude application of the usual chemotherapeutics, determinations of resistance should unconditionally be made. The role of the laboratory is to establish and confirm the use of the proper chemotherapeutic agents. Determinations of resistance are also significant in preventing the misuse of chemotherapeutics. Misuse leads to a constant increase of toxic and allergic reactions and a dangerous change of intestinal flora. The criterion whether the results in vitro can be applied as a guide for therapy will be whether there is agreement between the determinations of resistance and the results of treatment.

Chronic Ulcerative Colitis Due to Pollen Allergy with Six Case Reports. A. H. Rowe, A. Rowe Jr. and K. Uyeyama. Acta med. scandinav. **152:**139-151 (no. 2) 1955 (In English) [Stockholm, Sweden].

The cases of four women between the ages of 28 and 48, one 33-year-old man, and one 12-year-old girl with chronic ulcerative colitis are described. Pollen allergy was the sole cause of seasonal chronic ulcerative colitis in three of these six patients. Pollen allergy was the major and possibly the sole cause in one of the three other patients, while food allergy in addition to pollen allergy was considered in the two remaining patients. Perennial desensitization with a multiple pollen antigen containing all of the pollens of major or moderate importance in the patient's home, recreational, and work environments, even though skin tests yielded negative results, controlled the seasonal chronic ulcerative colitis (July to December) in one patient for 14 years, except for a mild recurrence of colitis of two weeks duration after pollen therapy had been discontinued for eight months. Pollen therapy controlled the seasonal chronic ulcerative colitis in three other patients for three years, two years, and one year respectively. No elimination diet and no drugs were employed in these four patients. In the remaining two patients considerable improvement was obtained with pollen therapy and the addition of strict elimination diet. Determination of possible pollen allergy depends on a history of occurrence or exaggeration of chronic ulcerative colitis in the pollen season. Positive reactions to skin tests may be absent. Confirmation of pollen allergy depends on good results obtained with prolonged proper desensitization. When pollen allergy is the sole cause of chronic ulcerative colitis, perennial desensitization with multiple antigens, without drugs or elimination diet, will gradually produce good results in three to nine months and excellent results in one to three years. In patients in whom food and rare drug allergies are associated with pollen allergy, these associated allergies require control. In the presence of secondary infection and anemia, administration of antibiotics and sulfonamide compounds and blood transfusions may be required. Administration of antispasmodics and antidiarrheal drugs, in addition to antiallergic therapy, may be necessary for brief periods only or not at all. Corticotropin (ACTH) and cortisone, which may exert a favorable effect on fulminating symptoms of ulcerative colitis, were not available for the treatment of the authors' patients. With the control of food and pollen allergy, the administration of antibiotics, and other valuable adjuncts, surgical treatment of chronic ulcerative colitis will be required less frequently. In the course of the last seven years ileostomy and colectomy were advised in only two of the authors' patients with chronic ulcerative colitis. One was a young woman who cooperated in antiallergic therapy; after four months of treatment, however, obstruction of the ileocecal valve made surgery indispensable. The other patient was well controlled with the elimination of allergic foods for three years; she insisted on taking some excluded food, was given cortisone to allow the ingestion of these foods, and within two weeks perforation of the sigmoid occurred, which necessitated ileostomy and colectomy.

Effect of Yogurt with Prune Whip on Constipation. F. P. Ferrer and L. J. Boyd. Am. J. Digest. Dis. **22:**272-273 (Sept.) 1955 [Fort Wayne, Ind.].

The yogurt available now is a product of pasteurized milk inoculated with strains of Lactobacillus bulgaricus and Streptococcus thermophilus. It removes putrefactive and other organisms from the intestinal tract by changing the flora. Yogurt has essentially the same effect as acidophilus milk, except that (1) it is stable for a longer period—two weeks as compared with two days—and (2) it has a uniform creamy consistency and pleasant taste, whereas acidophilus milk may have a sour milk taste. Prunes likewise act as a natural intestinal stimulant in promoting intestinal elimination without purgation. The authors used a combination of 5.5 parts of prune-whip and 2.5 parts of yogurt in the treatment of 194 patients with constipation, who were being cared for in wards and who had a typical cross section of chronic geriatric illnesses, except that the gravely ill were not included. The average age of the patients was 71.6 years. Over 46% were diabetic. No laxatives were required during the period of administration of the prune-whip-yogurt in 187 or 95.8% of the patients, whereas the remaining 7 patients still required laxatives. An increase in the blood sugar level but little or no glycosuria resulted in 22% of the patients with diabetes. During the period of the prune-whip-yogurt administration, the patients showed improvement in skin tone, in seborrheic dermatitis, in chronic ileus, and in diabetic ulcers. Furthermore, the morale was improved, and there were fewer requests for additional food.

The Mortality in Australia from Cancer for the Period 1946 to 1950. H. O. Lancaster. M. J. Australia **2:**235-239 (Aug. 13) 1955 [Sidney, Australia].

This report is a summary of the vital statistics on cancer in Australia for the years from 1946 to 1950. The term cancer is used to include any malignant growth, that is, carcinoma, sarcoma, and melanoma, but the leukemias and Hodgkin's disease are not included. There have been some improvements in the death rates from cancers at all ages, but the death rate from cancer of the lung has steadily increased, especially in males. This is the only important rise in the death rates among the common cancers. Of the cancers showing definite trends, improvements were noted for those of the uterus, buccal cavity, esophagus, stomach, liver, and larynx. Previous upward trends in the death rates from cancer of the ovary and breast appear to have ended.

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SURGERY

Pulmonic Stenosis with Left-to-Right Ventricular Shunt. S. Contro and P. Brostoff. Am. Heart J. **50:**543-550 (Oct.) 1955 [St. Louis].

The occurrence of pulmonic stenosis is reported in eight patients, ranging in age from 5 to 24 years, with a left-to-right shunt between the ventricles, an oxygen increase from right atrium to ventricle of at least 1.1 vol. %, a pulmonary flow greater than the systemic, and a systemic arterial oxygen saturation of at least 90%. The salient clinical features of these patients were normal development, absence of cyanosis at rest, reasonably good adaptation to the congenital anomaly, and absence of clubbing. The vascularity of the lungs was normal or increased, even when the second pulmonic sound was markedly diminished or absent, and the classical murmur of pulmonic stenosis was heard. The electrocardiogram showed strain of the right side of the heart, usually associated with evidence of right bundle branch system block. Patients with pulmonic stenosis and left-to-right ventricular shunt are presenting the clinician with a therapeutic dilemma, because pulmonic valvulotomy and/or infundibular resection may be deleterious by producing a left-to-right shunt of tremendous magnitude, actually causing the patient to bleed as it were into his lung and die in shock. Shunting procedures, the other surgical approach to pulmonic stenosis associated with ventricular septal defect, are not necessary, since the patient is acyanotic and has a good pulmonary flow. Since patients like those reported on usually tolerate their congenital anomaly quite well, it would appear to be wiser to await the future development of more practical surgery for septal defect.

Direct Vision Intracardiac Surgical Correction of the Tetralogy of Fallot, Pentalogy of Fallot, and Pulmonary Atresia Defects: Report of First Ten Cases. C. W. Lillehei, M. Cohen, H. E. Warden and others. Ann. Surg. **142:**418-445 (Sept.) 1955 [Philadelphia].

Ten patients, all of whom were seriously ill with Fallot's tetralogy, were operated on by direct vision intracardiac curative procedures, using controlled cross circulation for the necessary interval of total bypass of the heart and lungs. Through application of the low flow concept to this perfusion technique, important simplifications in method became possible. Based upon the azygos flow experimental studies, the authors perfused these patients during their bypass interval at a rate of blood flow approximately 1/6 to 1/4 of the resting cardiac outputs for normal individuals of comparable size and weight. These flow volumes varied from 23 to 29 ml. per kilogram of body weight per minute. In the 10 patients so managed, the heart and lungs were totally bypassed from 6 to 21½ minutes. All of the six patients who survived have a normal clinical appearance and are asymptomatic postoperatively. The systemic artery oxygen saturations are also within normal range in all. The first two patients operated upon were subjected to recatheterization of the right side of the heart from six to seven months after the operation. The first patient remains asymptomatic but has a small left to right shunt high in the right ventricle. The second has normal oxygen contents and pressures demonstrating that complete anatomic and physiological restoration to normal can be achieved in a patient born with these tetralogy defects. Two more complicated defects were also successfully managed by these corrective techniques. The first of these concerned a 22-month-old girl with complete atresia of the main pulmonary artery at its origin, in whom it was possible to close the ventricular septal defect and to create a new opening at the top of the outflow tract in the right ventricle to which the pulmonary artery was anastomosed. The other patient was a 10½-year-old boy with a pentalogy of defects in whom simultaneous atrial and ventricular cardiotomies were well tolerated. The authors feel that the operation is the method of choice for all patients with the tetralogy of Fallot who are in need of surgical treatment. For the lesser degrees of disability, they recommend temporary postponement of any surgical operation and periodic reevaluation of the patient's cardiac status. For the patient currently in need of surgical treatment for whom an intracardiac procedure is not available, they recommend an anastomotic operation without the opening of the pericardium. This operation provides palliation and does not interfere with an intracardiac operation should it be deemed necessary subsequently.

Middle-Lobe Syndrome. G. E. Lindskog and H. C. Spear. New England J. Med. **253:**489-495 (Sept. 22) 1955 [Boston].

A typical case of atelectasis with chronic pneumonitis involving the right middle lobe, which has been classified as a clinicopathological entity called "middle-lobe syndrome" by Graham and co-workers, is described in a 25-year-old woman. The patient's chief complaint was a chronic productive cough of several years' duration. For four years prior to admission to the Grace-New Haven Community Hospital in Connecticut, she had had increasingly frequent and prolonged upper respiratory infections. Repeated sputum examination had been negative for acid-fast bacilli by smear and culture. Iodized oil (Lipiodol) bronchograms revealed atelectasis and extensive saccular bronchiectasis of the middle lobe, which were confirmed at lobectomy. Although the pathogenesis of the clinical, radiological, and bronchoscopic manifestations of the middle-lobe syndrome have been clarified, an accurate differential diagnosis is often difficult or may be impossible before operation. The problem of differential diagnosis is illustrated by the reports of six cases in two men and three women between the ages of 57 and 76 years and a 7-year-old boy who were admitted to the same hospital in the course of the preceding 12 months. The lesions in these six patients included bronchogenic carcinoma; atelectasis and organizing pneumonitis secondary to tuberculous hilar lymphadenitis; parenchymal tuberculosis; chronic abscess with organizing pneumonitis; acute pneumonitis, with resolution; and lipid pneumonia. Each of the six cases constituted a distinct pathological entity, the sequelae of which may be progressive and fatal, but each patient presented some clinical and radiological features in common with middle-lobe syndrome. The definitive diagnosis of middle-lobe syndrome can be made only by surgical intervention, which was performed in all seven patients, and after examination of the resected specimen, but not on the basis of clinical, bronchoscopic, and radiological findings.

The Place of Parasternal Curettage in the Treatment of Breast Cancer. H. Redon and J. Lacour. Presse méd. **63:**1173-1176 (Sept 10) 1955 (In French) [Paris, France].

The authors treated 100 patients with cancer of the breast by radical amputation with removal of the parasternal lymph nodes. In 20 instances they also performed supraclavicular emptying, in addition to axillary and internal mammary dissection. Patients who had had previous radiation therapy were not excluded from the group. Sixty had tumors of the internal or median portion of the breast, and 40 had them in the external quadrants. No attempt was made to preserve cartilage, because the authors had observed three cases of painful chondritis in a prior series of patients. There was no operative mortality in the present series; four patients had aseptic pleural effusions that were resorbed spontaneously, and three had considerable disunion, severe enough in one instance to require secondary grafting. Such disunions have become exceptional since the routine use of closure under tension. It was found that the internal mammary nodes were invaded in 26% of the cancers of the internal quadrants or the median portion and in 15% of those of the external quadrants. They were the only site of metastases in two cases. There were four cases of involvement of the supraclavicular nodes. Follow-up of these patients has ranged from six months to two years, and the 19 patients who have died have been studied from various points of view. It appears that removal of the internal mammary nodes does not aggravate the prognosis, as evidenced by a comparison of this series with 100 patients in whom the Halsted operation alone was performed. However, the rate of relapse and of metastasis formation in the first postoperative year was definitely greater in the patients who were given this broadened surgical treatment. It is possible that the greater trauma of this method is a contributing factor.

Agammaglobulinemia: An Approach to Homovital Transplantation. R. L. Varco, L. D. MacLean, J. B. Aust and R. A. Good. Ann. Surg. **142:**334-345 (Sept.) 1955 [Philadelphia].

While the establishment of enduring homovital grafts has long been a challenge to medical science, the facts are that organ transplants between persons (with the exception of homozygotic twins), despite initial acceptance, ultimately are rejected by the host. Since the immunologic theory of antigenicity in the donated organ provoking an antibody reaction-rejection in the host has more current support than other hypotheses, the possibilities in that experiment of nature which is congenital agammaglobulinemia seemed worthy of investigation. Four persons with gamma globulin deficits of varying magnitudes received skin grafts from unrelated eugammaglobulinemic adults of dissimilar blood type. Homotransplantation of skin proved possible in two children with congenital agammaglobulinemia. In both of these children extensive immunologic studies were carried out, which revealed that the underlying deficiency was an immunologic paralysis. Each of these two children, in whom the total amount of gamma globulin was less than 15 mg. per 100 cc., continued to maintain the integrity of the grafted cutaneous layer, the time elapsed since grafting in one being 13 months and in the other 4 months. A third child, in whom agammaglobulinemia was of a transient nature, and an adult with the acquired form of agammaglobulinemia, after an initial take, slowly rejected the alien skin transplant.

Metabolic Changes and Therapeutic Considerations in Bilateral Adrenalectomy. I. G. Graber and P. Beaconsfield. Brit. M. J. **2:**704-708 (Sept. 17) 1955 [London, England].

There is a consensus that hyperactivity of the adrenal cortex is responsible for the metabolic changes produced by surgery and anesthesia. These changes include sodium retention, increased potassium excretion, high potassium/nitrogen ratio, and urine of low specific gravity. The superimposition of bilateral adrenalectomy on a surgical procedure would thus produce further problems and difficulties in the body economy. From this point of view, three consecutive patients with carcinoma of the breast and widespread metastases were studied for three days before they underwent simultaneous bilateral adrenalectomy and oophorectomy and for three weeks after the operation. Observations in these patients revealed postoperative changes similar to, but different in detail from, those found after surgery and anesthesia in patients who were not subjected to adrenalectomy. In the absence of adrenal glands, the metabolic changes effected by increased pituitary activity modified by cortisone therapy were sodium retention, a constant potassium excretion, low potassium/nitrogen ratio, and urine of high specific gravity. Surgical patients other than those undergoing bilateral adrenalectomy enter a phase of diuresis after the period of sodium retention and then return to a normal preoperative pattern. The patients who were subjected to adrenalectomy also went through a postoperative period of sodium retention, but this was followed by a period of permanent sodium diuresis. In the early phase of this latter period the percentage excretion of water, sodium, and potassium tended to remain slightly below the preoperative level. The potassium/nitrogen ratio was well below the preoperative level and the glomerular filtration rate was increased during this early phase of sodium diuresis. The late phase of sodium diuresis was characterized by an increase in the percentage excretion of water, sodium, and potassium equal to or above the preoperative figures, with a maintenance of the high glomerular filtration rate. The potassium/nitrogen ratio during this period rose to above the preoperative level and to values much higher than those found during the early phase of sodium diuresis. The patients who underwent adrenalectomy thus differ from other surgical patients in that no period of convalescence restores a normal hormonal balance. Instead, a state is reached that is reminiscent of adrenal cortical hypofunction (Addison's disease), modified by the administration of cortisone. The cortisone has the renal effect of increasing the glomerular filtration rate while maintaining the percentage excretion rate of water, sodium, and potassium above that of the earlier periods after operation. The use of desoxycorticosterone acetate is probably unnecessary in the immediate postoperative period and may even be harmful by prolonging the period of sodium and water retention. The use of desoxycorticosterone acetate or the newer fluorohydrocortisone may prove beneficial in the late diuretic phase. Patients who undergo adrenalectomy have an increase of antidiuretic substance in the blood; this substance is antagonistic to cortisone. Signs of adrenal insufficiency, low blood pressure, abdominal pain, and scanty urine with high specific gravity and low sodium content require increased cortisone therapy regardless of the maintenance dose.

The Treatment of Tuberculosis of the Spine by Evacuation of the Paravertebral Abscess and Curettage of the Vertebral Bodies. M. C. Wilkinson. J. Bone & Joint Surg. **37B:**382-391 (Aug.) 1955 [London, England].

Fourteen children and 51 adult patients with tuberculosis of the spine without paraplegia were treated by evacuation of the paravertebral pus and curettage of the tuberculous focus in the vertebral body. This procedure, which is referred to as central curettage, was carried out safely with antibiotic cover. Nine of the 14 children had disease of the thoracic spine and 5 of the lumbar spine; 34 adults had disease in the midthoracic or lower thoracic region; and 17 had disease in the lumbar region. Patients were selected for operation mainly because the prognosis without surgical intervention seemed doubtful or poor. The patients were followed up for from one to five years after the operation. Of the 65 patients, 60 are at home and well and most of them engaged in their normal activities. Of 51 (78%) who have a stable and comfortable spine, 36 have bony ankylosis of the affected spinal segments, 4 have re-formed vertebral bodies, and 11 have firm fibrous ankylosis. The remaining 14 patients still have an unstable spine, though some of these are much improved. Relapses occurred in 10 patients who required readmission for further treatment. Six of these patients were among the earliest operated on, when the supply of streptomycin was scanty and when the operation was also sometimes inadequate. After further treatment, 5 of these 10 patients have recovered with solid ankylosis; one child is at home and well but has severe deformity; and 4 patients are still receiving treatment in hospital. There has been no death among the patients treated by central curettage. The duration of the treatment of these patients was considerably less than that formerly necessary. These results represent a considerable improvement over those hitherto reported.

Hypothermia in Surgery: Analysis of 100 Clinical Cases. H. Swan, R. W. Virtue, S. G. Blount Jr. and L. T. Kircher Jr. Ann. Surg. **142:**382-400 (Sept.) 1955 [Philadelphia].

The authors review observations on 100 patients undergoing 105 operative procedures during general hypothermia. Direct vision intracardiac procedures were carried out in 59, closed intracardiac procedures in 21, and operations unrelated to heart disease in 20 patients. For achieving direct vision intracardiac operation, hypothermia is both safe and effective in congenital lesions that can be repaired by an approach through the right side of the heart, with occlusion times of 8 minutes or less at body temperatures not lower than 26 C (78.8 F). The mortality rises sharply when these limits are exceeded. The authors consider it the method of choice in the treatment of isolated valvular or infundibular pulmonary stenosis and of interatrial septal defect. The technique seemed favorable for the reduction of the operative risk in patients with congenital heart disease characterized by deep cyanosis or by hypertrophied overactive hearts. It may be less well tolerated or even of no benefit in the presence of strain on the left side of the heart. The technique is both effective and safe as a method of allowing temporary regional or organ ischemia to achieve a bloodless field. The patients with cirrhosis had pulmonary hypertension and hepatocellular dysfunction. Those with aneurysm were to have resection of thoracic or abdominal lesions. The cerebral lesions were either aneurysms of the internal carotid or hemangioma. In these, temporary occlusion of all blood flow to the head was performed intermittently by means of tapes around the vertebral and carotid arteries. The patients with visceral cancer required massive extirpative procedures. Acute hypothermia above 26 C appears to involve a

low risk in human subjects, provided many precautions are observed. The authors found the effect of adequate ventilation so convincing that they subject all patients to deliberate hyperventilation throughout the cooling, operative, and warming periods. They also found that hypothermic anesthesia is a two man job; one must constantly give undivided attention to the maintenance of ventilation; to his associate go all the other multiple activities associated with modern anesthesia. Coronary air embolism has been one of the serious problems of open heart surgery. If air is trapped in the left side of the heart, it will almost surely find its way into the coronaries. The crux is to trap no air, and the authors describe the technique that they have devised to achieve this. Of the 22 deaths, 14 could possibly be related to hypothermia. Ventricular fibrillation and its sequels are the chief cause of death. The authors combat ventricular fibrillation as follows: Manual cardiac compression is continued until the myocardium is pink and of good tone. Electric defibrillation with metal electrodes delivering 170 volts and about 2.5 amperes for 0.1 or 0.05 seconds placed at the apex and over the base of the heart is tried next. Two or three shocks in fast succession are usually successful; if not, 3 to 5 ml. of potassium chloride solution is injected by coronary perfusion. If this chemical defibrillation is not successful, electric shock is repeated, after manual compression has dispelled myocardial cyanosis. If the heart become flabby with very fine fibrillations, adrenalin chloride can be injected into the left auricle, and, if this coarsens the fibrillation, the stage is set for successful electric defibrillation. The authors conclude that general hypothermia is of sufficient safety to warrant further use and evaluation.

NEUROLOGY & PSYCHIATRY

Immediate Prognosis in Cerebral Apoplexy. E. Skinhøj. Nord. med. **54:**1313-1315 (Aug. 25) 1955 (In Danish) [Stockholm, Sweden].

Study of 1,000 cases of cerebral apoplexy at the neurological department of Frederiksberg Hospital showed no sex difference in the immediate prognosis in cerebral apoplexy. Lethality increases with increasing age, except that it is somewhat higher than expected in young patients. In these patients there are usually no relatively benign thromboses but considerably more dangerous hemorrhages, most often on the basis of a grave disease such as chronic nephritis with severe hypertension. The general state of health before cerebral apoplexy is surprisingly unimportant, and a preceding cerebral accident does not significantly lessen the chance of survival after repeated apoplexy. Conditions that decisively lessen the chance of survival are loss of consciousness, whether initial or later; hypothermia; pathological respiration, especially of Cheyne-Stokes type; respiratory or cardiac insufficiency expressed by cyanosis; and, first and foremost, terminal hyperpyrexia. Less than one-fifth of the patients who improve in the first 24 hours die and only about one-fourth of those die whose condition is not directly aggravated at this time. With the exception of terminal hyperpyrexia, there is no symptom that carries an unconditional sentence of death.

Causes of Death in Cerebral Apoplexy. T. Lyager. Nord. med. **54:**1315-1317 (Aug. 25) 1955 (In Danish) [Stockholm, Sweden].

Of 1,000 patients with cerebral apoplexy at the neurological department of Frederiksberg Hospital, 443 died. Comparison of the anatomic changes and the case records shows that 224 patients, or 68% of 331 patients, died as a direct result of the apoplexy; 156 had cerebral hemorrhage and 68, thromboembolism in the brain. In 107 patients, the primary or complicating extracerebral affections were so grave that they must be considered the direct cause of death. Thromboembolism in extracerebral vessels, found in 71 patients, is regarded as the direct cause of death in 50. The fact that 42% of the 156 who died from cerebral hemorrhage and only 18% of the 68 who died from thromboembolism died on the first day after admission might suggest that cerebral hemorrhage has a more violent course. The apparently marked tendency to thromboembolism may testify for increased application of anticoagulants in cerebral apoplexy. Of the 22 cases of death from pneumonia, only three deaths occurred after January, 1948, which is attributed largely to treatment with antibiotics and also to the steadily increasing treatment directed against disturbances in the respiratory passages.

Hypophysectomy in Man: Further Experiences in Severe Diabetes Mellitus. R. Luft, H. Olivecrona, D. Ikkos and others. Brit. M. J. **2:**752-756 (Sept. 24) 1955 [London, England].

Hypophysectomy was performed in 10 men and 10 women with diabetes mellitus of 13 to 22 years' duration and diabetic vascular complications that had been diagnosed one to seven years earlier. The aim of the surgical intervention was to eliminate those anterior pituitary factors that animal experiments have shown to have a diabetogenic action. All patients had diabetic retinopathy; blood pressure was generally raised; and albuminuria and proteinuria were present. Seven patients died within one day to 19 months of the operation. The surviving patients were followed up for 3 to 43 months. Substitution therapy consisted of the administration of thyroxin, estrogens and androgens, and adrenocortical hormone or desoxycorticosterone acetate. Women were placed on a diet containing 1,400 to 1,700 calories daily and men on one containing 1,600 to 2,000 calories. The patients were given a daily maintenance dose of 8 to 24 units of long-acting insulin. In the surviving patients, hypophysectomy was followed by a fall in blood pressure and a decrease in heart volume. In patients who had calcification of peripheral vessels before the operation, this condition was not affected, but no calcification occurred postoperatively in other patients. Capillary fragility was normal after the operation in all patients except one. A definite decrease in albuminuria and in glomerular filtration was achieved with the operation, but the effective renal plasma flow remained unchanged. These observations can be taken as a sign of a lowering of tonus of the vessels of the glomeruli, which in turn can be considered as a favorable effect of the operation on the renal circulation. No signs of progression of the renal disease were observed, though the authors' findings did not permit any conclusions as to improvement in the condition of the kidneys. The visual capacity improved in some patients and the retinal changes did not progress. The limited period of observation and the small number of patients do not permit conclusions as to the therapeutic value of hypophysectomy for the vascular complications of diabetes mellitus, but results obtained so far are encouraging.

Safeguards in Angiography. A. Ver Brugghen. J. Internat. Coll. Surgeons **24:**310-315 (Sept.) 1955 [Chicago].

While it is conceded that cerebral angiographic examination is a valuable diagnostic tool, it admittedly causes serious complications such as transient or permanent hemiplegia, the decerebrate state, and even death. Complications have ranged from 3 to 10% and the mortality rate from 0.2 to 3.5%. The author feels that these high rates no longer occur today. He has had little trouble with cerebral angiographic studies. He describes his method and the results he obtained with it in the first 150 angiograms taken at the Presbyterian Hospital in Chicago. Ninety per cent of these were done by the author himself, and 10% by residents. All of these patients were given 35% Diodrast, and so far there have been no untoward reactions. All studies were done with the patient under sodium Pentothal-oxygen anesthesia with an intratracheal tube. After transport from the anesthesia to the roentgen room, the patient's head was put on the Sanchez-Perez machine. The skin of the neck was prepared, and the common carotid artery was entered percutaneously between the sternum and the lower border of the thyroid cartilage. When a satisfactory jet of blood was obtained, a piece of polyethylene tubing, with Luer locks at both ends, was attached to the needle by the operating surgeon, while the nurse attached a 10 cc. glass syringe with Luer lock, a metal plunger, and rings for the fingers. The syringe was emptied as rapidly as possible of 8 to 10 cc. of 35% Diodrast. As the plunger neared the last third of the barrel, the order was given to start the series of plates. The Sanchez-Perez machine, which is a rapid plate changer, was set to take six plates in five seconds. The lateral view was made first, and,

unless there was some special problem, anteroposterior views were not taken. Both lateral and anteroposterior views were taken in about half of the patients, that is, in those in whom a tumor was seen or strongly suspected. In a few cases arteriograms of the common carotid and vertebral arteries were combined on one side. Bilateral studies were made in only very few cases and were nearly always restricted to lateral views. No patient was given more than 20 cc. of 35% Diodrast on either side of the brain. If more than one injection is required, an interval of several minutes should be allowed. No untoward effects occurred in this series of 150 patients. While this may represent a lucky series, the author feels that an experienced, constant team will insure maximum efficiency.

Incidence of Infection Among Contacts of Poliomyelitis Cases. D. M. Horstmann, R. W. McCollum and A. D. Mascola. J. Clin. Invest. **34:**1573-1580 (Oct.) 1955 [New York].

The apparently erratic spread of poliomyelitis with rarely more than one case in a family puzzled the early investigators, but later it became apparent that the majority of infections with poliomyelitis virus were mild or inapparent and, therefore, went undetected. With the introduction of tissue culture techniques into poliomyelitis research, it has become possible to carry out more extensive virological studies and to relate virus isolation or its absence to the immune or antibody status of the persons tested. The studies described were carried out during a poliomyelitis epidemic in two rural counties in which the over-all attack rates were 193 and 280 per 100,000, respectively, with mortality rates of 16 and 8.2 per 100,000. As soon as possible after a patient with poliomyelitis was hospitalized or reported to the health officer, inquiries were made among the family members and neighborhood contacts. Of the 91 contacts with which this report is concerned, 54 were household contacts and 37 were daily contacts, the latter being playmates or close neighbors of the poliomyelitis patients. Virus isolations as a measure of infection were correlated with immune status, that is, the presence or absence of antibodies. If only antibody negative (and therefore presumably susceptible) contacts are considered, the infection rates for those under 15 years of age were 100% for household contacts and 87% for daily contacts. The epidemic was due to type 1 virus, and type 1 virus was isolated with greater frequency from those with symptoms than from those who remained asymptomatic. Many of the asymptomatic group were demonstrated to possess antibodies to the family type of virus; when these were eliminated, there was no significant difference in the ease of virus isolation from individuals with symptoms as compared with those who remained asymptomatic. In analyzing the clinical response to poliomyelitis virus infection among family associates of patients, it was found that the ratio of inapparent to apparent infection was approximately 3:1 (and not higher than 7:1). It is suggested that the high incidence of apparent infections in the group studied (compared with the ratio for the general population) might be related, in part at least, to factors of exposure and dosage: in a family of a patient, exposure is of a high degree, the dosage of virus is presumably large, and the incidence of paralytic and nonparalytic infections is correspondingly high. On the basis of virus isolations and serologic evidence, poliomyelitis infection may be said to be as contagious as measles among susceptible persons in a family setting.

A New Method of Activation of the Electroencephalogram: Scalp Electrical Stimulation (SES). M. Gozzano, L. Sinisi, G. Tonini and R. Vizioli. Electroencephalog. & Clin. Neurophysiol. **7:**407-414 (Aug.) 1955 [Montreal, Canada].

A new method of electroencephalographic activation, scalp electrical stimulation, is described. It consists of the application to the scalp of rectangular pulses of low voltage and high frequency. It was found that this method increases the recording of electrical abnormalities, particularly in patients with intracranial tumors. In such cases, the electrical stimulation of the scalp was of considerable help in localization. The stimulating current was well tolerated by the patients, and the results suggest that the method would be helpful in routine electroencephalography of intracranial tumors.

GYNECOLOGY & OBSTETRICS

Further Results Obtained in Treatment of Cancer of Cervix with Radiogold: A Progress Report. W. A. Allen, A. I. Sherman and A. N. Arneson. Am. J. Obst. & Gynec. **70:**786-790 (Oct.) 1955 [St. Louis].

Allen and his associates began the use of radioactive gold for the irradiation of the parametrium in carcinoma of the cervix five and one-half years ago. A year ago they reported the results obtained with radioactive gold and compared these results with those obtained by roentgen and radium rays in the years from 1950 to 1953 inclusive. The present report is concerned with the same patients, plus those treated during 1954. Initially, only patients who were good operative risks and had stage 1 lesions were treated with radioactive gold, the treatment consisting of the parametrial injection of gold followed by radical Wertheim hysterectomy and pelvic lymphadenectomy. Later, poor operative risks were treated with only radiogold and radium. In the original group of 100 patients with stage 1 and stage 2 lesions, there were only 30 patients who were not subjected to a radical hysterectomy. Of the 49 stage 1 and 2 patients treated with radiogold during 1954, only 21 were subjected to operation, the remaining 28 being treated with only radiogold and radium. No stage 3 patients have been operated on as yet. Radium has been used in virtually all stage 1, 2, and 3 lesions. Patients subjected to operation generally received less than 5,000 mg.-hr. of radium, whereas those not operated on were given from 6,000 to 8,000 mg.-hr. The amount of radiogold injected was usually 100 to 130 mc. divided equally between the two sides. The results obtained are described and discussed, but the authors arrive at no definite conclusion, except that they seemingly obtained better results in patients treated with radiogold than in patients treated during the same period with roentgen rays and radium or in patients treated prior to this study with roentgen rays and radium.

The Significance of Basal-Cell Hyperactivity in Cervical Biopsies. G. A. Galvin, H. W. Jones and R. W. Te Linde. Am. J. Obst. & Gynec. **70:**808-821 (Oct.) 1955 [St. Louis].

The term basal cell hyperactivity is one of several that have been applied to the epithelial aberrations in the uterine cervix, which, while not manifestly benign, yet do not satisfy the criteria of malignancy. The term is used for that histological picture in which the epithelial layer approximates in thickness that of the normal portio vaginalis and in which there is an abnormal number of immature cells so that normal stratification is interfered with and normal architecture is partially destroyed. There are various degrees of epithelial deviation, depending upon the number and anaplasia of the immature cells and varying from slight alteration in the normal surface epithelium to a picture simulating carcinoma in situ. To facilitate classification and comparison, the authors arbitrarily divided basal cell hyperactivity into three stages, in which stage 1 shows only slight divergence from the normal epithelial layer, stage 2 represents more conspicuous changes, and stage 3 approaches the microscopic picture of surface carcinoma. The material for this investigation was assembled from the gynecologic outpatient clinic of the Johns Hopkins Hospital during the four-year period terminating in December, 1954. Cervical biopsies, although obtained quite freely, were not routinely taken but were obtained only when signs or symptoms aroused suspicion of cervical abnormality. Initially, 343 patients with a diagnosis of basal cell hyperactivity were referred to the authors for further study. The review of the original biopsies disclosed that the histological changes in 101 were insufficient to justify such a diagnosis, in 20 the changes were those of carcinoma in situ, and in 7 there was actual invasion of the stroma by malignant cells. These cases, as well as an additional 24 in which the follow-up investigation was inadequate, were excluded, and there remained 191 patients for study. The authors arrive at the following conclusions: 1. Basal cell hyperactivity, when found in cervical biopsies, requires more thorough investigation of the cervix, as carcinoma in situ will be found eventually in a substantial number of these cases. Noninvasive cancer was found in 33, or 17%, of the 191 patients in-

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vestigated. 2. The probability of this eventuality increases sharply with the degree of basal cell hyperactivity. While only 2% of patients classified as having stage 1 basal cell hyperactivity were eventually proved to have carcinoma in situ, 65% of those in stage 3 finally showed this histological picture. 3. Evaluation of a selected group of 11 of the patients seems to indicate that basal cell hyperactivity may progress to carcinoma in situ. 4. Complete regression of even a marked degree of basal cell hyperactivity represents a warning that this condition must be differentiated from carcinoma in situ and must never be diagnosed or treated as such.

An Experimental Program with Colposcopy. L. C. Scheffey, W. R. Lang and G. Tatarian. Am. J. Obst. & Gynec. **70:**876-888 (Oct.) 1955 [St. Louis].

The principle of colposcopy consists of stereoscopic visualization of the cervix under magnification with direct lighting. Changes in the cells and cellular architecture of the surface epithelium are detectable with surface enlargement. The colposcope used magnifies 10 and 20 times. It is a binocular instrument mounted on an adjustable stand with a transformer in the base. By means of a side lever, magnification can be changed from 10 to 20 times without refocusing. When correctly placed, the colposcope "looks" at right angles upon the surface of the cervix previously exposed by a speculum. The instrument has at attachment for taking 35 mm. Kodachrome pictures. This is an excellent method of securing a permanent record of normal and abnormal findings. The authors have used the instrument for 450 colposcopic examinations. They first insert the speculum with the patient in the usual lithotomy position and then adjust the colposcope. The cervix is viewed first as is; then after gentle cleansing; next after the application of 3% aqueous solution of acetic acid the better to delineate detail; and, last, aqueous iodine (Schiller test) is applied. After the authors had become familiar with the normal cervix under the magnifying colposcope, they began work on patients referred from the gynecologic and obstetric clinics because of clinical abnormalities or an unusual cytological report. Their impressions are based on observations on 168 patients studied during the last year. Fifteen of these had squamous cell carcinoma; 7 had recurrent or unarrested lesions; lesions that proved benign on histological examination were observed in 23; and the remaining 123 patients also had benign lesions. While colposcopy will never replace the fundamental means of diagnosing cervical cancer, that is, history, pelvic examination, cytological smear, biopsy, and fractional curettage, it is of value as an accessory method in the early diagnosis of cervical cancer. The Papanicolaou smear technique should be used in connection with the procedure, for it will point to specific areas for biopsies, but it will never replace the latter for the definitive diagnosis upon which therapy depends. Neither can colposcopy eliminate circular or cone biopsies for microscopic study of all areas when this is clinically indicated. The authors did not diagnose a single malignancy with the colposcope alone. They became greatly impressed with the educational advantages of the instrument. The excellent color photographs made possible by the instrument have added much to the visual education of students and of the house and attending staffs.

Diverticulosis of the Fallopian Tubes: A Clinical and Roentgenologic Study. A. M. Siegler. Fertil. & Steril. **6:**432-442 (Sept.-Oct.) 1955 [New York].

During 1941 to 1953, a total of 1,160 hysterosalpingograms were performed on women complaining of infertility. A diagnosis of tubal diverticulosis was made in 19 patients, an incidence of 1.6%. The ages of these 19 patients ranged from 24 to 43 years. Only three of these women had had normal pregnancies prior to investigation for infertility. There had been 11 spontaneous abortions and 2 tubal pregnancies. Tubal diverticulosis was associated with endometriosis in two patients, pelvic inflammatory disease in two, myoma of the uterus in eight, cervical stenosis in three, and retrodisplaced uterus in two patients. Dysmenorrhea was present in eight of the women. Diverticulosis may be suspected in a woman in the fourth decade of life who has a history of unexplained involuntary sterility of five years or over, no previous pelvic inflammatory disease, no palpable adnexal masses, and no increase in temperature or sedimentation rate. Endometrial biopsy should not be suggestive of tuberculosis. The diagnosis of tubal diverticulosis was made primarily by salpingography. The diverticula were found chiefly in the isthmic, isthmoampullary, and isthmocornual regions of the tubes, and they were usually multiple, resembling the branches of a tree. There was a significant inconsistency in the results of tubal insufflation and of hysterosalpingography; diverticula are not revealed by tubal insufflation. If tubal diverticulosis is discovered incidentally at laparotomy and the tubes are grossly normal, they should not be operated on. A woman who has a long-standing history of infertility with bilateral isthmic occlusion due to diverticulosis might be a candidate for reconstructive surgery; reimplantation might be attempted. Preoperative culdoscopic examination might be helpful in the selection of the patient likely to benefit from tubal plastic surgery.

Hormonal Therapy in Gynecology. J. E. Hall. Connecticut M. J. **19:**723-726 (Sept.) 1955 [New Haven, Conn.].

The use of hormones is often abused in gynecology as in other branches of medicine. Hormones are not miracle substances, but each hormone has specific actions and these should be known before it is administered. Certain gynecologic disturbances may be helped by the use of the right hormone in proper dosage, but hormones are of little value in many conditions for which they have been employed. Harmful results may follow their improper use. However, if the proper substance is employed, the hormones will prove of value in many gynecologic problems. Thus estrogens are helpful in the menopause, atrophic vaginitis, and the suppression of lactation but are of questionable value in dysfunctional uterine bleeding, amenorrhea, dysmenorrhea, endometriosis, and malignant states. Progesterone may be effective when the corpus luteum of pregnancy is surgically removed and of questionable value in dysfunctional uterine bleeding, amenorrhea, corpus luteum deficiency, and dysmenorrhea. The androgens are helpful in treating the menopausal symptoms, when estrogens are contraindicated, and in the suppression of lactation. Their value is questionable in treating frigidity and malignancy. Gonadotropins have no proved value in gynecologic problems. Thyroid is effective in menstrual abnormalities that are associated with deficient function of the thyroid. Cortisone may be of value in treating certain specific menstrual disturbances due to deficiency of the follicular phase of the menstrual cycle and may also serve as an adjunct in treating advanced malignancy.

Maternal Rubella: Results Following an Epidemic. D. L. Brawner. J. M. A. Georgia **44:**451-454 (Sept.) 1955 [Atlanta, Ga.].

Twenty-six pregnant women contracted rubella in the course of an epidemic of rubella, which occurred in the spring of 1952 in Chatham County, Georgia. Twenty-two of these women were followed to the end of gestation, and therapeutic abortion was done in four women. Rubella was diagnosed by history alone in 5 cases and on the basis of an examination by a physician in the other 21 cases. In seven women the rubella occurred during the first eight weeks of gestation; three of these gave birth to normal infants; three infants showed anomalies, and one infant was stillborn at seven months. Of the three with anomalies, one had congenital heart disease and multiple facial anomalies; another had harelip, cleft palate, and congenital heart disease; and one had bilateral cataracts. Of the eight women who had the rubella between the eighth and the twelfth week of gestation, one gave birth to a child with harelip and cleft palate and the other seven women gave birth to normal infants. There were mild abnormalities in the infants of two of the five women in whom the rubella occurred during the second trimester, but the nature and mildness of these defects make it doubtful that the rubella played a causal role in their development. The infants of the two women who were in the last trimester of pregnancy during their attack of rubella were free from anomalies. These cases of maternal rubella indicate that the first eight weeks of pregnancy is the crucial period in which rubella may cause serious fetal damage.

PEDIATRICS

Narcosis and the Fetal Brain. C. B. Courville. Bull. Los Angeles Neurol. Soc. **20:**97-101 (Sept.) 1955 [Los Angeles, Cal.].

The introduction of anesthesia into obstetrics has been hailed as a great advance in medicine, but a more critical evaluation of the effects of analgesic and anesthetic drugs on the fetus casts some doubt on this conclusion. It has been learned that all pharmaceutical agents that have a narcotic effect inevitably depress the fetal respiratory center, usually in excess of that of the mother. The well-being of the fetus, whose intrauterine existence is maintained in a state of relative anoxemia, a state that is accentuated during the process of delivery, is thereby placed in jeopardy. Should the narcotic agent be used in excess or should some concomitant exist which also favors the development of anoxemia, the sum total of all contributing factors may result in a disaster. Although body tissues as a whole tolerate quite well even a fairly severe degree of anoxemia without serious damage, it is quite a different matter with the immature and unduly vulnerable tissues of the fetal brain, notably the cerebral gray matter. Even a transitory insult, although obscured for the time being by the fact that breathing was soon established, may indelibly stamp its mark upon the infant's brain. This purely narcotic depression is rarely severe enough to result in the death of the infant. It seems reasonable to conclude, however, that the effects of narcosis on the fetal brain resulting in postnatal apnea may be responsible in some cases for at least the lesser degrees of motor disability, mental deficiency, and epilepsy. In some cases it may also be a contributing factor in the production of the gross motor syndromes observed in cases of cerebral palsy. It is true that these complications of obstetric narcosis are relatively rare, but every preventable case is a tragedy to the victim and his family.

Cerebral Palsy: Where Next? R. V. Fuldner. A.M.A. Arch. Neurol. & Psych. **74:**267-279 (Sept.) 1955 [Chicago].

The birth and maternal gestational records of 204 children with athetoid quadriplegia, spastic quadriplegia, spastic hemiplegia, or spastic paraplegia were reviewed. No abnormal findings with regard to pregnancy, labor, or the respiratory status of the newborn infants were recorded in 70 cases. The cause of cerebral palsy in many of the 134 tabulated cases was quite evidently fetal oxygen deprivation. It appears that hypoxia provided a common basis for the varying mechanisms of cord entanglement, dystocia, premature placental separation, and delayed onset of respiration to produce brain damage. Other causes of brain damage, such as bilirubinemia and maternal illness, were relatively infrequent. There was almost no evidence to support the concept of cerebral palsy's being the result of a heredofamilial defect. At least 103 cases, or more than half the total, seem to have been anoxic in origin, and, since data supplied by many hospital records are inadequate, the incidence of fetal anoxia is probably higher than this figure suggests. The quantitative aspects of hypoxia must be considered in any evaluation of its pathogenic capacity. Keith's follow-up studies on infants with asphyxia or delayed respiration included only one patient in whom the period of apnea is stated to have been in excess of 15 minutes. It now turns out that the period of apnea in cerebral palsy, where stated, tends to higher levels. The lethal potentiality of prolonged hypoxia with respect to the cerebral neurone was recently demonstrated by the case of a boy with spastic quadriplegia commencing after his imprisonment, at the age of 3, in an unused icebox for seven hours with minimal ventilation. A pet kitten that also underwent the experience died a week after their release, and autopsy showed complete destruction of the cerebral cortex. The goal in the treatment of cerebral palsy must eventually be prevention. A clearer understanding of the mechanisms of neonatal asphyxia needs to be gained by controlled studies of infants with complicated deliveries. It is essential that further data be obtained from a representative variety of obstetric sources and that follow-up procedures provide for accurate diagnosis of the children under investigation.

Interstitial Plasma Cell Pneumonia in Premature Infants. H. Laursen. Nord. med. **54:**1285-1288 (Aug. 18) 1955 (In Danish) [Copenhagen, Denmark].

Interstitial plasma cell pneumonia is practically always without symptoms till late in the course. The disease affects only premature and debilitated infants and occurs mainly from the sixth week to the fourth month of life. The typical symptoms are marked tachypnea, dyspnea, and cyanosis. Auscultatory changes are slight. The temperature is usually normal and may be subnormal. Roentgenologically there is diffuse infiltration in both lungs. According to the literature, the mortality is from 22% to 90%. In one of the three cases reported by the author, the patient survived. Autopsy in the other two cases showed typical pathognomonic changes. Histological examination of pulmonary tissue revealed structures corresponding to the pneumocystitis carnii described by Vaněk and Jirovec. Drugs such as Atebrin and Plasmochin can be effective in plasma cell pneumonia; the usual chemotherapeutics are without avail. The incubation period is thought to be about one month. Infection is assumed to be either peroral through food contaminated from the sputum or feces of animals (insects may also transmit the infection) or through inhalation of pneumocysts from dust or adult carriers. The best prophylaxis is isolation of the sick children and children who have been exposed to infection.

New Treatment of Infantile Enuresis with Antispasmodics and Vitamin E. S. Gianolla. Minerva pediat. **7:**756-759 (June 30) 1955 (In Italian) [Turin, Italy].

Biaxin, a combination of vitamin E, diethylstilbestrol, a derivative of glyceryl trinitrate, and testosterone, was used in the treatment of 19 boys with severe enuresis that had not responded to previous treatments. The patients, whose age ranged from 10 to 16 years, were chosen from the 350 boys living at the Don Bosco Boys' Village in Rome. It was ascertained that the disturbance had not appeared in these boys as the consequence of disease, surgical intervention, or severe trauma. Hyperexcitability was observed in 13, dermographia in all 19, hyperreflexia in 15, slight disturbances of the cardiac rhythm in 3, and cystitis in 4. Alterations in the tonus and movements of muscles and joints, renal disease, spina bifida, or sacralization of the fifth lumbar vertebra were not present. The boys were given 20 drops of Biaxin in the morning when they arose, at 5 p. m., and again at 8:30 p. m. when they went to bed. A 10 to 12 day treatment period gave good results in some boys; for others the therapy had to be continued for as long as 20 days. Recovery was obtained in 95% of the patients; 13 of them ceased to urinate at night after two or three days of treatment. The general condition was improved in all the boys, who also became more confident in themselves and more interested in their environment and in the social life at the Village. The only side-effect—slight enlargement of the breasts—disappeared a few days after the therapy was discontinued. At the time of writing, more than three months later, the good results were still present. In only one patient did the disturbance reappear occasionally.

DERMATOLOGY

Accidental Vaccinia. H. B. Ansell. J. Maine M. A. **46:**223-226 (Aug.) 1955 [Portland, Maine].

Three cases of accidental vaccinia are reported. The first patient was a woman who had an erythematous, papulovesicular, and pustular eruption involving the face, scalp, neck, breasts, antecubital and popliteal areas, and several fingers. The patient stated that her son had been vaccinated about two weeks before the onset of her illness. The eruption resembled smallpox, and while the involution was slow, there was practically no residual scarring after recovery. This patient, who had been vaccinated in childhood, had a history of eczema, asthma, and urticaria. The second patient stated that her baby had been vaccinated 11 days prior to the onset of her eruption. This patient had never been vaccinated, but she too had a history of eczema. Her lesions were diagnosed as multiple accidental vaccination. The third

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patient, a 4-year-old boy, had an eruption involving his lip and left elbow. He had sustained an abrasion of his left elbow the day before he was vaccinated in the left deltoid area. A week after the vaccination, he fell and injured his lower lip, and two days later his mother noticed the development of a lesion on the lip. A diagnosis of autovaccination of the left elbow and lower lip was made. Because of the symmetry and the extensive extent of the eruption in the first patient, the author believes that this was an example of hematogenous spread of the vaccinia virus. Case 2 is an example of surface inoculation in a susceptible person, and case 3 is considered as surface inoculation in a vaccinated individual who had sustained abrasions both prior to and subsequent to vaccination. Patients with skin lesions who have never been vaccinated or who have not been recently vaccinated should avoid contact with newly vaccinated persons.

Isonicotinic Acid Hydrazide in Treatment of Lupus Vulgaris. M. Bhattacharyya and L. M. Kakoti. Indian M. Gaz. **89:**580-583 (Oct.) 1954 [Calcutta, India].

Two patients with lupus vulgaris were treated with daily doses of 200 mg. of isoniazid for a period of 12 weeks. The patients received the ordinary hospital diet and were permitted to move about as they pleased. One of the two patients, a 25-year-old man, achieved complete clearance of the lupus lesions, and the other patient, a 16-year-old girl, showed great improvement. Although observations on only two patients do not permit conclusions, the authors feel that, in a country where sunshine is plentiful, lupus vulgaris might be successfully managed with this simple treatment.

UROLOGY

Technique of Percutaneous Renal Biopsy in the Prone Position. R. C. Muehrcke, R. M. Kark and C. L. Pirani. J. Urol. **74:**267-277 (Sept.) 1955 [Baltimore].

Since 1954, when the authors first reported on their new technique of percutaneous needle biopsy of the kidney with the patient in the prone position (J. A. M. A. **156:89** [Sept. 4] 1954), 153 biopsies have been done. The exact position of the kidney was found with the aid of an excretory urogram and a fine exploring needle. The biopsy specimen was taken with Franklin's modification of the Vim-Silverman needle. A sandbag under the abdomen pushed the kidney against the back and provided hemostasis through pressure after biopsy. Neither serious hemorrhage nor dissemination of infection occurred in the patients, aged 10 to 66 years, on whom the biopsies were performed. Biopsies were repeated on 10 patients, and 3 of these had three serial biopsies without adverse sequelae either from a functional or structural viewpoint. Kidney biopsy proved to be of great value by either correcting or confirming clinical diagnoses of renal disease. Exact pathological diagnoses were made providing the background for etiology, diagnosis, and prognosis. Kidney biopsy also was useful in obtaining cultures of organisms from the kidneys, in following the natural history of diseases involving the kidneys through serial biopsies, in discovering new diseases of the kidneys, in assessing the effects of drugs on renal and cardiovascular disease, in studying renal cytology and cytochemistry, in studying the morphology of the kidneys by the electron microscope, and in obtaining data that may clarify present concepts of the physiology and pathophysiology of the kidneys.

Nephrocalcinosis and the Acidity of the Urine. T. B. Reynolds. J. Urol. **74:**257-266 (Sept.) 1955 [Baltimore].

Renal tubular acidosis is a condition that leads to chronic acidosis, potassium deficiency, bony dissolution, nephrocalcinosis, and stone formation. It is easily recognizable because of the abnormally high urine pH (around 6.5), which fails to drop when acid is ingested. Urinary tract infection with a urea-splitting organism as a cause of the abnormal pH can be ruled out by the low ammonium content of the urine. Though the fundamental renal tubular fault has not as yet been elucidated, the abnormal findings are explicable on the basis of chronic loss of body buffer salts. Oral treatment with an inexpensive mixture of 100 gm. each of sodium and potassium citrate per liter of water with syrup of orange as a flavoring agent (two teaspoonfuls three times daily) will have the following effects: relief of the systemic acidosis with restoration of normal blood biochemical values, and usually a sense of well-being; restoration of intracellular potassium stores, a normal serum potassium level, and relief of muscle weakness; termination of the process of bony dissolution with recalcification of bone and healing of pseudofractures; disappearance of hypercalcuria; and interruption of nephrocalcinosis and stone formation. Since the urine pH remains around 6.5, calcium excretion in the urine should be closely followed with the aid of Sulkowitch's test during the initial months of therapy while the bones are being reconstituted. When it is felt that this process is complete, a low-calcium diet should be adhered to, to minimize calcium excretion. Three illustrative cases are described in women between the ages of 19 and 48 years. Paralytic attacks secondary to potassium depletion are not uncommon in renal tubular acidosis and were observed in two of these patients. No further paralytic attacks occurred after the institution of the treatment with the mixure of sodium and potassium buffer salts. None of the patients were followed long enough to indicate whether any decrease in the nephrocalcinosis can be expected, but none of them had progression of their calcification nor any further stone passage.

Papillomas of Bladder: Analysis and After-Examination of 183 Cases. F. Lund and F. Lundvall. Ugesk. læger **117:**1123-1131 (Aug. 25) 1955 (In Danish) [Copenhagen, Denmark].

From 1929 to 1952, 183 patients with papilloma of the bladder (147 men and 36 women, aged mostly between 60 and 70) were admitted in Bispebjerg Hospital. The average period of observation was 92 months for men and 113 months for women. The symptoms were hematuria, constant or intermittent, painful micturition, and pollakiuria. Six patients were not operated on, in 22 transurethral electrocoagulation alone was done, in 138 transurethral electrocoagulation and extirpation, and in 17 transvesical interventions were performed. The postoperative mortality was 4%. Most recurrences come in the first year. Recurrences after a symptom-free period of many years are not rare. The danger of malignant transformation is considerably greater with primary multiple papillomas than with solitary papilloma. Follow-up of 165 patients revealed recurrence in 43 out of the 125 with a solitary papilloma, in 7 as carcinoma; and in 29 of the 40 with multiple papillomas, in 8 as carcinoma. The cardinal symptom, hematuria, must never be neglected; other symptoms from the urinary tract may also indicate closer examination of the entire tract. The earlier the patients are treated, the better the prognosis as to both the total number of recurrences and the number of malignant recurrences. During the five-year period after operation, control every three months in the first year, twice during the second year, then once yearly is advised.

The Treatment of Tuberculous Infections of the Genitourinary Tract. J. K. Lattimer. J. Urol. **74:**291-300 (Sept.) 1955 [Baltimore].

Chemotherapeutic treatment of tuberculosis of the genitourinary tract was practiced in 625 patients in the course of seven years. The authors emphasize that chemotherapeutic treatment of genitourinary tuberculosis should be continued for one uninterrupted year. They believe that the treatment should always consist of a combination of drugs. Combined treatment with two drugs (streptomycin and aminosalicylic acid) or three drugs (streptomycin, aminosalicylic acid, and isoniazid) was more effective than treatment with any one drug alone in converting positive urines to negative. Only time will tell whether prolonged mild chemotherapy with two drugs for two years may prove more effective than intensive chemotherapy with three drugs for one year, or whether one will find it best to use streptomycin and aminosalicylic acid for one year and isoniazid and aminosalicylic acid for a second year. At present a therapeutic trial is conducted with a combination which consists of 1 gm. of streptomycin twice a week, 100 mg. of isoniazid three

times daily, and 5 gm. of sodium aminosalicylate three times daily. This program is continued for one year. The results so far obtained from this regimen are the best the authors have seen to date. Surgical interventions, such as partial nephrectomy, prostatectomy, and epididymectomy, are deferred more and more, because of the success of chemotherapy. The authors feel that any patient who does have an operation on the urinary tract because of tuberculosis should have chemotherapy for one year in addition to the operation, with four months of therapy preceding the operation and eight more months of treatment after the operation. Results so far obtained with chemotherapeutic treatment of tuberculosis of the genitourinary tract justify the statement that the prognosis of this formerly fatal disease has been definitely improved.

THERAPEUTICS

Problem of Bacterial Resistance in Antimicrobial Therapy of Tuberculosis. H. C. Sweany, F. P. Dunbar and E. Wood. Dis. Chest **29:**260-274 (Sept.) 1955 [Chicago].

Sweany and associates made a study to determine the time of emergence of resistance in a series of far-advanced cases of tuberculosis, which it was thought would remain positive for at least a year and in which resistance could be studied with various drug combinations, especially streptomycin and isoniazid; aminosalicylic acid and isoniazid; and aminosalicylic acid, isoniazid, and streptomycin. Out of a large number of cases, only 13 could be followed long enough to reveal any worthwhile information. In the other cases, the sputum turned negative before such information could be obtained. Another object was to find out, if possible, the combination of drugs that gives the best and most lasting therapeutic effect as well as the combination that delays the emergence of resistance the longest. The preliminary aims have not been completely realized, but a few trends have been observed that may be of some use in the administration of future drug regimens. Reports made in the past indicate that resistance develops to isoniazid within one and a half to three months. The resistance to streptomycin has been reported to develop in two to four months in about 70% of the cases when used alone. Resistance to aminosalicylic acid when used alone has been reported to develop in about 50% of the cases within three to four months. By combining the three drugs in different combinations emergence of resistance is delayed, owing to what is thought to be a double mutation, which is found to be much rarer than the mutants resistant to the drugs individually. Accordingly, streptomycin and isoniazid together prolonged the emergence of resistance at least to twice the time of either of the drugs alone, sometimes much longer. Streptomycin and aminosalicylic acid together prolong the time of the emergence of resistance severalfold. Aminosalicylic acid and isoniazid also prolong the development of resistance much longer than when the respective drugs are used separately, and even longer than any other combination studied. From the meager data at hand the combination of the three drugs together does not seem to offer any advantages not possessed by the various two-drug combinations. Furthermore, there is the advantage of having a potent drug available if resistance should develop to any two. A plan of treatment has been suggested that would use streptomycin and isoniazid in critical or panic cases; streptomycin and aminosalicylic acid in ordinary pulmonary tuberculosis and ordinary complications; and isoniazid and aminosalicylic acid where resistance has developed for streptomycin.

The Toxic Effects of Phenylbutazone (Butazolidin): Review of the Literature and Report of the Twenty-Third Death Following Its Use. E. F. Mauer. New England J. Med. **253:**404-410 (Sept. 8) 1955 [Boston].

The twenty-third death following the use of phenylbutazone, a drug resembling aminopyrine in chemical structure, is reported. The patient was a 48-year-old woman, who had taken 35 tablets, 100 mg. each, of phenylbutazone over a period of 22 days because of a painful knee. At this time a rash appeared; her physician discontinued the drug and gave an injection of corticotropin (ACTH). Despite the prompt withdrawal of the drug, nausea, vomiting, burning in the mouth with difficulty in swallowing, and generalized aching appeared. When the woman was hospitalized, her temperature was 100.4 F (38 C), and there was a diffuse, blotchy, red rash and epigastric tenderness. Abdominal pain increased, and, when rigidity of the upper abdomen developed, laparotomy was performed, which revealed an acute duodenal ulcer. The rash became purpuric, and other signs of capillary fragility were related to reduction in prothrombin level, which did not respond to the administration of fresh blood and vitamins K and K_1. On the 8th hospital day, blood smears yielded evidence of bone-marrow involvement; on the 10th day, there was jaundice, and severe intractable diarrhea began; and by the 12th day, the skin had begun to exfoliate. During the last 10 days of life the exfoliation involved the entire face, the neck, the thorax, and all extremities. The temperature was generally 100 to 103 F (37.7 to 39.4 C), but on the 22nd hospital day it suddenly went over 108 F (42.2 C). The patient became comatose and died 2 days later, 28 days after the first sign of toxic reaction following the phenylbutazone therapy. Death was due to an acute necrotizing process, which involved the skin, causing exfoliative dermatitis; the liver, leading to diffuse toxic hepatitis; and the colon, causing mucosal necrosis and superficial ulceration. Similar lesions were present in the vagina, urinary bladder, and elsewhere in the intestinal tract. The literature concerning the toxicity of phenylbutazone shows that the serious reactions are not related to dosage or duration of treatment. They may occur after the drug has been withdrawn. There are no known methods of predicting an impending reaction. At present there are no specific means of treating reactions. In advertisements, phenylbutazone has been recommended for gouty arthritis, rheumatoid arthritis, osteoarthritis, psoriatic arthritis, spondylitis, fibrositis, bursitis, scapulohumeral periarthritis, myositis, neuralgia, and sciatica. If the drug had curative powers in any of these conditions, a risk might be justified, but phenylbutazone is only an analgesic somewhat similar to the abandoned aminopyrine.

Anaphylactoid Shock Due to Penicillin. H. Cruz Hernández and C. R. Rosa-Febles. Bol. Asoc. méd. Puerto Rico **47:**323-326 (Aug.) 1955 (In Spanish) [Santurce, Puerto Rico].

Anaphylactoid shock secondary to an injection of penicillin, or to local use of the antibiotic is a grave and often fatal condition, more frequent than is believed. Symptoms of shock with cyanosis, dyspnea, pulmonary edema, urticaria, angioedema, stupor, and convulsions appear shortly after use of the antibiotic and follow a rapidly acute course. The patients are critically ill. The therapy consists of the use of epinephrine, oxygen, antihistamine drugs, and administration of a 5% dextrose solution intravenously. General measures include warmth and posture of the patient. A case of acute course with recovery of the patient with the aforementioned treatment is reported.

Gangrene of Arm Following Accidental Intra-Arterial Injection of Somnifene (Barbital Preparation) in Violent Mental Patients. E. Arruda. Hospital **48:**209-224 (Aug.) 1955 (In Portuguese) [Rio de Janeiro, Brazil].

Four cases of dry gangrene of the arm following accidental intra-arterial injection of Somnifene (a barbital preparation) are reported. The patients were given an injection of Somnifene into the arm when they were admitted to the hospital as mental cases in a state of violent agitation. Intravenous injection was intended. On the morning following administration of the injection, the patients exhibited loss of use of the arm. An irreversible syndrome of arteritis obliterans, with acute pain, edema, local hyperthermia, and cyanosis, rapidly progressed into dry gangrene that made amputation of the arm necessary. A histological study was made on portions of arteries, veins, and muscles taken from the amputated arm of one of the patients. The veins were normal. A diagnosis of endarteritis and infiltrative exudative myositis was made. The author was able to reproduce this circulatory syndrome in monkeys that had an injection of Somnifene into the axillary artery.

First Clinical Trials with Prednisone (Metacortandracin or Meticorten). G. Bickel. Schweiz. med. Wchnschr. **85:**859-861 (Sept. 3) 1955 (In French) [Basel, Switzerland].

Prednisone (Meticorten) was given a therapeutic trial in 13 patients, 9 of whom had chronic rheumatoid arthritis, 3 had bronchial asthma, and 1 had lipid nephrosis. The total dose of the drug administered varied from 120 to 2,415 mg., and the duration of treatment varied from 8 to 140 days. In contrast to other workers, the author considers a massive daily dose of from 20 to 25 mg. of prednisone, instead of one of 30 to 50 mg., given in four divided doses, as sufficient for patients with rheumatoid arthritis who previously were treated with cortisone. This dose may be reduced gradually to one of 15 to 20 mg. daily. A daily dose of 20 mg. was sufficient for the control of bronchial asthma in two patients who had been treated previously with a daily dose of 80 to 100 mg. of cortisone. In a third patient with bronchial asthma who was not treated previously with cortisone, a massive dose of 60 mg. of prednisone was given for two days, 40 mg. were given for four days, and then 20 mg. daily. Results obtained in these patients with rheumatoid arthritis and bronchial asthma suggest that the antiinflammatory and antiallergic action of prednisone is definitely superior to that of cortisone and hydrocortisone. Prednisone was effective in patients in whom cortisone was ineffective or had lost its effectiveness in the course of prolonged treatment. The undesirable side-effects resulting from prednisone were less pronounced than those resulting from cortisone, and they occurred less frequently after prednisone administration than after cortisone therapy; this applies particularly to the retention of water and sodium, thus permitting, as a rule, administration of prednisone without placing the patient on a salt-free diet. Prednisone, however, is not an "inoffensive cortisone," since, on the 45th day of treatment with a daily dose of 15 mg. of prednisone, a severe digestive disturbance with hematemesis occurred without any warning symptom in a 68-year-old patient with rheumatoid arthritis of 25 years' duration who had been treated with cortisone for four years without any digestive disturbance. Gastralgia developed in one-third of the author's other patients. The appearance of peptic ulcer and recurrences of ulcer were reported by other workers. The favorable end, as a rule, striking initial effect of the drug became less pronounced as treatment continued, thus requiring higher doses with a greater risk of undesirable side-effects. Prednisone did not prove to be superior to corticotropin (ACTH) or cortisone in the patient with lipid nephrosis who was given an initial daily dose of 80 mg. of prednisone, which was rapidly decreased to 30 mg. and later on to 20 mg.

Antibiotic Products of a Versatile Fungus. H. W. Florey. Ann. Int. Med. **43:**480-490 (Sept.) 1955 [Lancaster, Pa.].

Florey says that a fungus producing an antibiotic had been isolated by Brotzu at Cagliari in 1945, while he had been looking for antibiotic-producing micro-organisms in the sea near a place where there was an outflow of sewage, his idea being that possibly in this neighborhood organisms antagonistic to those in sewage might be developed. Brotzu grew the fungus on agar and showed that it produced an antibiotic active against a number of pathogenic bacteria. He considered the organism to be Cephalosporium acremonium. He grew the fungus on a liquid medium, into which it secreted the antibiotic, which he endeavored to separate. He made an active, though impure, extract, which, together with culture fluid, was used for the parenteral treatment of patients suffering from typhoid and from infection with Brucella melitensis. The preparations were also used for local application. In 1948 associates of Florey in Britain began study on the Cephalosporium isolated by Brotzu. It was found that the Cephalosporium fished out of the sea by Brotzu produces a variety of antibiotics. One of them, cephalosporin P, though inferior to several antibiotics, might conceivably be valuable in combating staphylococcic infection, although it has not yet been so tried in man. A second is a new kind of penicillin, of which some physical, chemical, and biological properties are substantially different from those described for any other penicillin. It is conceivable that it may be useful for the treatment of typhoid and in patients sensitive to penicillin G. It offers possibilities for the manipulation of the penicillin molecule for the production of other antibiotically active substances. There has also been isolated an antibiotic, cephalosporin C, which is possibly related in some ways to penicillin. It has, however, quite different physical and chemical properties and may have an application in medicine especially for the treatment of staphylococcic infections resistant to other antibiotics.

The Influence of Chemotherapy on Survival in Acute Leukemia. A. Haut, S. J. Altman, G. E. Cartwright and M. M. Wintrobe. Blood **10:**875-895 (Sept.) 1955 [New York].

One measure of the effectiveness of therapy in the treatment of acute leukemia is its influence on longevity. The median survival was calculated for 103 of the 142 patients (children and adults) seen at the University of Utah College of Medicine from March, 1947, to March, 1954, and for 782 patients reported on in the literature. The records of all 142 patients seen at the authors' clinic were reviewed; in some cases, however, they were inadequate and had to be excluded largely because geographical considerations made it inconvenient for the patients to continue their attendance at the clinic. Another eight patients were excluded from the calculations because they had received inadequate trials of treatment, i. e., less than 10 days with folic acid antagonists, less than 7 days each with corticotropin (ACTH) and cortisone, and less than 14 days with 6-mercaptopurine. Patients who received x-ray, nitrogen mustard, urethan, Myleran, or radioactive phosphorus ("nonstandard therapy") or folic acid antagonists, corticotropin, cortisone, or 6-mercaptopurine ("newer therapies") in any amounts were considered as "treated." The others, 11 in all, including those receiving only blood transfusions and antibiotics, were considered as "untreated." Antibiotics and blood transfusions, however, were administered in each case, treated or untreated, according to the appropriate indications. Data for comparison were provided by 782 cases in series taken from the literature; single case reports were not included, and series limited to cases treated before the antibiotic era were not considered in order to avoid dissimilarity with the authors' group. These patients, children and adults, were also classified as treated (639) or untreated (143). Separate analyses were made for the several modes of therapy. It could not be shown that the newer therapies significantly increased the total survival in these groups. The median survival, however, in patients who had at least one complete remission was increased from four and one-half to eight months, which was found to be a statistically significant difference. Failure to find an increase in the total survival, which is rather surprising, may be accounted for in various ways, such as the possibility that the use of chemotherapeutic agents may fail to alter the course of acute leukemia in some instances while prolonging it in others; the fact that, of the series suitable for analysis found in the literature, only one was of later date than 1952; and, finally, that the use of 6-mercaptopurine was not adequately represented in the survey. Failure to show that therapy prolongs the course of acute leukemia in a large unselected group of patients, however, should not lead to a defeatist attitude in treatment or in the study of the effects of new antileukemic agents. Many patients treated by modern methods live to enjoy temporary improvement for several weeks or months. This reduction in morbidity, which does not appear in the statistics under discussion, should not be overlooked.

Accidents in the Course of Heparin Therapy: Reactions of Allergic Type. G. Massone. Minerva ginec. **7:**491-493 (July 31) 1955 (In Italian) [Turin, Italy].

Allergic types of phenomena occurring during heparin therapy may be primary, caused by hypersensitiveness to the anticoagulant, and acquired, caused by sensitization. The former are generally rare and not too grave, and the latter are commoner and more severe and are characterized by shock, bronchospasm, and cyanosis. The author reports the occurrence of an allergic reaction due to hypersensitiveness in a 49-year-old woman to whom he gave 50 mg. of heparin intravenously for thrombophlebitis of the left leg secondary to a gynecologic operation. The symptoms—a transitory feeling of warmth, hyperemia of the skin and mucosa, diffuse urticaria-like signs, headache, and nausea—dis-

appeared after the administration of antiallergic preparations and epinephrine. He observed the onset of nausea, sweating, and dyspnea followed by paresthesia to the extremities, bronchospasm, cyanosis, and shock in another patient, with thrombophlebitis that developed during the puerperium, who had tolerated well heparin therapy for five days. The administration of antihistamines, cardiovascular analeptic drugs, and oxygen in a closed circuit restored the patient to normal in two hours. In addition to phenomena caused by hypersensitiveness and sensitization to heparin, there are also allergic reactions that are both primary and secondary at the same time. These are the cases in which signs of intolerance that appear after the first injection are so mild as to be overlooked or underestimated, but they become progressively more severe during the subsequent injections. Such reactions can be defined as manifestations of a very slight primary hypersensitiveness that is followed by a marked sensitization. Massone observed this type of reaction in two patients who were benefited by the administration of antiallergic preparations and epinephrine.

PATHOLOGY

Further Experience with a New Blood Medium for the Cultivation of Mycobacterium Tuberculosis. M. S. Tarshis, W. A. Weed, P. C. Kinsella and others. Am. J. Pub. Health **45:**1157-1161 (Sept.) 1955 [Albany, N. Y.].

In earlier investigations it had been demonstrated that a medium containing plain agar, glycerol, outdated bank blood, and penicillin was satisfactory for the cultivation of tubercle bacilli under routine diagnostic conditions. It was found also that the medium was useful for determining the susceptibility of tubercle bacilli to streptomycin and isoniazid. The studies described here compare the new blood medium with the Lowenstein-Jensen medium under routine diagnostic conditions. It was found that the number of positive cultures obtained and the average time of first appearance of growth were slightly better on the blood medium than on the Lowenstein-Jensen medium. The number of tubes contaminated was much less for the former than the latter medium. This is attributed to the presence of penicillin. The chief advantages of the blood medium are economy, simplicity of preparation, and ability to grow tubercle bacilli from small inoculums, easily, recognizably, and in a short time. The ingredients are readily available, and fresh mediums can be prepared in a few minutes. Refrigerated mediums have proved stable in tightly sealed screw-cap tubes for as long as four months. All these factors should encourage a wider use of cultural methods for the bacteriological diagnosis of tuberculosis.

RADIOLOGY

The Vascular Pattern as an Aid to the Diagnosis of Bone Tumours. A. C. Begg. J. Bone & Joint Surg. **37B:**371-381 (Aug.) 1955 [London, England].

Roentgenograms taken at the end of an injection of 20 cc. of 50% iodopyracet (Diodone) solution into the bones of the leg indicated the extreme vascularity of the bones, particularly near an epiphysis, and emphasized the extraordinary capacity of the minute periosteal vessels. The nutrient artery of a long bone appears to play little part in its nourishment and may be regarded as a vestigial structure indicating the situation of the fetal diaphysis and the most avascular region of the adult bone. The vascular pattern of bone tumors may be investigated by arteriography after injection of the contrast medium into the appropriate artery. For lesions of the head and neck, the carotid or vertebral arteries may be used, for the shoulder girdle or the arms the subclavian artery, for the forearm the brachial artery, for the pelvic bones the abdominal aorta (preferably below the origin of the renal arteries), and for the thigh the common femoral artery or the superficial femoral or profunda femoris artery. The arteries of the leg are usually well shown by injection into the superficial femoral artery, but injection of the dorsalis pedis or posterior tibial arteries may be required to show the vessels of the foot. The examination is easily and quickly carried out by direct arterial puncture with the aid of local anesthesia and injection of 35% iodopyracet (Diodone) solution; a 70% solution is required for the aorta. A tourniquet applied distally at the appropriate level is often helpful. Sometimes, if a hemangioma is suspected, the injection of the contrast medium may be made directly into the lesion. Six illustrative cases are described in five women between the ages of 20 and 78 years and in a 39-year-old man, in whom a study of the vascular pattern of suspected bone tumor provided useful information by assisting both the diagnosis and the planning of treatment. The pathological diagnosis of some tumors, notably osteosarcomas and hemangiomas, may be made with such assurance that possible dissemination of the tumor by biopsy may be avoided.

Roentgenologic Observations in the Acrosclerotic Form of Generalized Scleroderma. A. Leszler. Fortschr. Geb. Röntgenstrahlen **83:**353-365 (Sept.) 1955 (In German) [Stuttgart, Germany].

It is now generally realized that scleroderma is not limited to the skin but is a systemic disease involving the vascular and the connective tissues. It may cause extensive and characteristic changes in various internal organs. The 22 patients studied by the author included 19 women and 3 men, and ranged in age from 36 to 74 years. The disease had existed for from 1 to 39 years. All these patients had the so-called acrosclerotic form of scleroderma, and in many it had begun with symptoms suggesting Raynaud's disease. In three of the patients the disease was limited to the skin, and the roentgenologic examinations failed to reveal involvement of other organs. In two of these patients the disease had existed for only one or two years. In 7 patients only one other organ besides the skin was involved, and in 12 several organs were involved. The involvement of the internal organs occurs late, the author observing it chiefly in those patients in whom the disease had existed for 10 and more years. Case histories are presented of the eight patients in whom the most interesting changes were observed. The author observed calcifications of the soft tissues in only three of his patients, but in one of these three the calcinosis was extremely severe. His observations confirmed the fact that the sclerodermic calcinosis is found chiefly in the regions of the joints—the shoulder, elbow, hand, and hip joints. Changes in the bone system were most frequent; they occurred in over 70% of the patients, appearing mostly in the form of osteoporosis of the bones of the hands and of osteolysis in the ungual phalanges. Involvement of the lungs, chiefly in the form of fibrosis and of bronchiectasis, was observed in 8 of the 22 patients. Cardiac enlargement was observed in four patients, but it could not be definitely demonstrated that this cardiac enlargement was connected with the scleroderma. The digestive tract was involved in half of the patients—lesions of the esophagus, in the form of mucosal atrophy, stiffness of the walls, cardiospasm, and disturbances in the esophageal passage being most frequent.

Treatment and Prevention of Leukopenia from Roentgen Therapy with a New Thymonucleic Acid Extracted from Fish Milt, Desoxyribose Tetranucleotide. R. Coliez, A. N. Loiseau and R. Sarfati. Presse méd. **63:**1137-1139 (Aug. 27) 1955 (In French) [Paris, France].

Desoxyribose tetranucleotide, a free, unstable nucleotide obtained from fish milt and developed in France under the name of Eucytol, has a marked stimulating effect on hematopoiesis, especially the regeneration of white blood cells. The authors administered it to 150 cancer patients undergoing deep irradiation therapy, all of whom showed blood disturbances and 50 of whom had a serious degree of leukopenia. From four to eight 0.05 gm. tablets of the product were given orally each day. The white blood cell count rose to safe or even normal levels within six to eight days. Thus the patients who had had severe leukopenia could continue their planned course of radiotherapy. Desoxyribose tetranucleotide, given simultaneously with a course of irradiation, constitutes an excellent prophylactic against sudden drops in the leukocyte count with the consequent necessity of interrupting treatment.

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BOOK REVIEWS

The Physician and the Law. By Rowland H. Long. Foreword by Milton Helpern, M.D., Chief Medical Examiner, New York City. Cloth, $5.75. Pp. 284. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1955.

There are not many books on the market that discuss those basic legal problems with which all physicians should have at least a nodding acquaintance. Furthermore, one can count on the fingers of one hand the books of this kind that are suitable for use by medical students. It is necessary to strike a happy medium between a book that is too simple and one that assumes a basic knowledge that does not exist. Mr. Long is to be commended both for his effort and his accomplishment. Although he has written primarily for the practicing physician, the book is suitable for use by medical students as well, and he has crowded a great many helpful suggestions and basic information into it. His discussion emphasizes the field of malpractice and the expert witness but also contains brief statements on such subjects as adoption, artificial insemination, medical licensure, workmen's compensation, blood tests, and the mentally ill. In order to cover these subjects even briefly, resort has been made to rather positive general statements. Such statements on almost any legal problem are subject to a certain amount of criticism. They do, however, have the merit of giving the physician a starting point, even though a legal brief could be written to support a contrary view. The author has not intended his book to be a legal treatise. References are comparatively few, many of them are to court decisions more than 20 years old, and they are placed at the end of chapters rather than as footnotes. This discourages their being read. The important thing, however, is that they are given, and the more curious physician and student may dig more deeply than the bare text if they wish to do so. There is a good glossary of legal terms, and the index is short but adequate. This book should serve as a primer satisfactory for practicing physicians and medical students.

Praktische Anatomie: Ein Lehr- und Hilfsbuch der anatomischen Grunlagen ärztlichen Handelns. Band I, Teil 2: Hals. Von Dr. T. von Lanz, o.ö. Professor der Anatomie, Direktor des anatomischen Instituts der Universität München, und Dr. W. Wachsmuth, o.ö. Professor der Chirurgie, Direktor der chirurgischen Universitäts-klinik und Poliklinik Würzburg. Cloth, 210 marks; subscription price, 168 marks. Pp. 549, with 322 illustrations. Springer-Verlag, Reichpietschufer 20, (1) Berlin W.35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1955.

This monograph on the neck is one of a series devoted to the applied anatomy of the human body. Volumes dealing with the arm and with the leg appeared in 1935 and 1938 respectively. These volumes are the scholarly product of the work of an anatomist and a surgeon extending over more than 20 years. Since practical considerations predominate, the anatomy of the neck is presented in the book largely from regional, topographical, and functional points of view. Systematic and developmental treatments are used to a lesser extent to supplement regional approaches. These varied treatments serve to set forth the anatomy of the living as the foundation of medical practice in general, and surgery in particular. The book is profusely illustrated with drawings, mostly in color, of exceptional quality. Illustrations are of sufficient size to facilitate location and identification of structures. In addition, there are a number of plates emphasizing relations and surface anatomy, usually by "phantom" views. This volume is so comprehensive in scope that it has no counterpart in the English language. Braus' German anatomic classic approaches it most closely in quality and manner of treatment. Eighty-five pages of bibliographic references are keyed to specific statements and illustrations in the text. The table of contents and index are extensive. The text is printed in large clear type on heavy glossy paper. Cover and bindings seem durable. Although written in German, which tends to limit its use as a textbook, the superior quality and variety of illustrations recommend it as an important atlas of regional and surgical anatomy. This volume should be available for reference in all anatomical and medical libraries.

Leonardo da Vinci: Das anatomische Werk mit kritischem Katalog und Abbildungen. Von Sigrid Esche. Ars Docta Band VIII. Half-cloth, 55 Swiss francs. Pp. 173; 175 plates. Holbein-Verlag, Rittergasse 19a, Basel, Switzerland, 1954.

The drawings of Leonardo da Vinci have been called the first truly scientific illustrations in the history of anatomy. Although he was occasionally misled by traditional concepts, his methods resulted in a large number of fresh and unprejudiced anatomical and physiological discoveries. In his drawings it is no exaggeration to declare that the body of man not only appears to function but changes. This accomplishment is adequately demonstrated in the present volume. For readers who are interested in one facet of the startling genius of a great representative of the Western world, this book will serve as a highly instructive and informative introduction. The critical notes add much to the background of the drawings.

Statistics of Therapeutic Trials. By G. Herdan, M. Sc., Ph.D., LL.D., Lecturer in Medical Statistics, University of Bristol, Bristol, England. Cloth, $10.50. Pp. 367, with 44 illustrations. Elsevier Press, Inc., 2330 Holcombe Blvd., Houston, Texas; 155 E. 82nd St., New York 28; 118 Spuistraat, Amsterdam-C, Netherlands [distributor for British Commonwealth, except Canada: Cleaver-Hume Press, Ltd., 31 Wright's Lane, Kensington, London, W.8, England], 1955.

This book is designed to serve as a guide for physicians who wish to apply statistical techniques in the evaluation of therapeutic data. Rather than serving as a condensed textbook on the statistics of probability applied to a subclass of medical statistics, it provides the practitioner with a reading knowledge of some simple approaches to the process of statistical inference. "Therapeutic statistics" is a summary term for the statistical procedures that are used in the design and evaluation of results of therapeutic trials carried out to compare different treatments. Thus, this term comprises both the statistical principles of the single trial, referred to as clinical statistics, and comparative therapeutics, which embodies the comparison of the results obtained at different times and places and in different classes of patients under varying conditions. In the effort to provide a quantitative measure for comparing the utility of alternative procedures, the magnitude of differences relative to their respective sampling errors are considered. This leads to a preliminary discussion that is handled in a rather superficial fashion. For example, one finds the statement on page 4, "Since even great differences might conceivably arise on pure chance, but with a very small probability which for all practical purposes might be neglected, we draw the dividing line between chance and significant differences at a specified multiple of the Standard Error [which is explained 78 pages later] to which corresponds a certain very small probability. Greater differences, having a smaller probability, are then considered as being due to a specific cause, that is, in our case, to the treatment in question." It might be pointed out that probability analysis precludes the neglecting of various levels of probability, thus the dividing line is a matter of arbitrary choice of the experimenter contingent on the level of significance selected. The magnitude of the difference between various measures, if related to the standard error, does not permit the direct assignment of causal factors but merely the nature of the association under similarly controlled experiments.

It is unfortunate that the section on statistical central values is written in such a manner as to be misleading, if not in error. Due to an error in proofreading, one finds on page 64 that other values of importance are the "medium," the mode, and the geometric mean. Only two characteristics of the arithmetic mean are found in this section. Omitted are other equally important attributes. On page 68 the author states, "The median is a use-

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ful form of average whenever there is an excessive number [what constitutes an excessive number?] of very small or very large observations. . . ." On page 69 the reader is alarmed to discover the statement that "In such a case, the mean does not represent the majority of observations or the most probable value." It might be pointed out that in no case does the mean represent the majority of observations or the most probable value. There is a measure of central tendency called the mode that presumes to express these characteristics. On page 73 is found the statement that "The duration of a disease is a useful criterion for the therapeutic comparison only if the fatality rate for that disease is small. Otherwise, it cannot be recommended for both clinical and statistical reasons." The student who wishes to apply the appropriate statistical techniques in the evaluation of data resulting from therapeutic trials might be concerned with the question of knowing the limits of the magnitude of the fatality rate that invalidate the usefulness of the criterion of the duration of a disease for therapeutic comparison.

The unorthodox presentation of the relation between the normal and the Bernoullian law that is found on pages 78 and 79 will be of interest to medical statisticians. Of particular interest is the statement that "The law which governs the random sampling fluctuations of frequencies, absolute or relative, of a particular outcome of a disease, is the *Bernoullian law*. The law which governs the distributions of counts and measurements due to biological variation is the *Normal law*, and the same law also governs the distribution of measurements affected by errors of observation and experiment, by themselves and in conjunction with biological variations. . . . The Bernoullian law governs only the random sampling variation of such counts; but since they are also affected by errors due to biological variations from patient to patient and with observational and experimental errors, the law of chance to be used when considering their distribution, is the Normal law."

The description of the concept of the coefficient of regression found on page 172 differs from that usually employed. In the linear expression $x=a+bt$ the coefficient b, which is the tangent of the angle of inclination, is usually designated as the incremental change in x per unit change in t rather than the coefficient of regression. The latter term is reserved usually to correlation analysis and the former to a series of values ordered by time. When this phrase is related to the statement found on page 173 that "For large samples b is normally distributed with σ_b as its standard deviation. . . ." the thought becomes clouded, insofar as it appears to be inappropriate to speak of a distribution of a single-valued function. The text is extensively documented. The footnotes are located at the end of each chapter. This book should serve as an excellent introduction to this important segment of medical statistics but will not equip the physician with a working knowledge of "statistics of therapeutic trials."

Angiographic Localization of Intracranial Masses. By Arthur Ecker, M.D., Ph.D., State University of New York, Syracuse, and Paul A. Riemenschneider, M.D., State University of New York. Cloth. $13.50. Pp. 433, with 413 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1955.

This book is a companion volume to "The Normal Cerebral Angiogram," which Dr. Ecker wrote in 1951. Like the previous book, it is a reference atlas, composed of a series of cerebral angiograms in proved cases of intracranial masses. Part 1, "Orientation," consists of a single chapter including diagrams of the normal cerebral vascular pattern in different projections, followed by line drawings and descriptions of the vascular displacements produced by masses in each region. Part 2, "Localization," illustrates the effect of a mass in various regions on the local vascular pattern. The classical appearance is generalized in diagrammatic form at the beginning of each chapter, and the subsequent roentgenographic illustrations are supplemented in many instances by reproductions of the plain films, pneumograms, surgical exposures, and pathological specimens. The arbitrary division of intracranial masses into 27 regional sites is justified on the grounds of the distinctive changes in the vascular pattern caused by a mass in each region. Thus, instead of referring to frontal lobe tumors as a group, seven subgroups of frontal masses are analyzed separately because the alterations they produce are different and distinguishable. The careful representation of the kind of vascular displacement produced by masses and of the vessels affected constitutes the core of this volume and its major usefulness.

A number of gaps must be mentioned. There is no discussion in the book of (1) the indications for carotid angiography; (2) the relative value of carotid angiography as contrasted with ventricular air studies; (3) the limitations of carotid angiography; and (4) the interpretative and diagnostic hazards. Virtually all workers with cerebral arteriographic studies have been confronted with a certain number of missed diagnoses and misleading appearances. A discussion by the authors of proved misdiagnoses might have been extraordinarily rewarding. Furthermore, the vascular pattern of the gliomas in angiography receives singularly little attention. The format is good, the type readable, and the line drawings accurate. As in "The Normal Cerebral Angiogram," all roentgenographic illustrations reverse the whites and blacks of the original roentgenograms. This departure from general American practice is not helpful. In spite of these criticisms, the authors have used the atlas method to elaborate a valuable reference source, to which cases under study may be compared. They emphasize their own practice of using a set of proved cases in their file for study of current problem cases in daily work and they suggest that this text may be employed in similar fashion. Used in this way, this volume should be of great value.

The Life and Work of Sigmund Freud. Volume 2: Years of Maturity, 1901-1919. By Ernest Jones, M.D. Cloth. $6.75. Pp. 512, with 15 illustrations. Basic Books, Inc., 59 Fourth Ave., New York 3, 1955.

The second volume of the proposed three volume biography of Sigmund Freud is divided into three parts. Part 1 deals with Freud in his maturity at the time when he waged his battle against the hostile world and no less hostile medical profession. He had disciples, but they were few, and even these were not in full accord with his views. Before long, dissensions and even defections developed. Prominent among the deserters were Adler, Stekel, and Jung. The second part of the book is particularly interesting and valuable because of the comprehensive, though brief, exposé of Freud's contributions to the subjects of infantile sexuality and the libido theory. These indeed are the most important elements in Freud's investigation of the "unconscious." The third part, analyzing Freud as a man, is excellent. What sort of person was the man who was able to penetrate the mystery of the unconscious? We discover, much to our surprise, that this man, who entertained most liberal, if not radical, views on the subject of sex, was "quite peculiarly monogamous." What is even more surprising is that this supreme psychologist was a poor judge of men. At least that was the feeling of all the disciples. The literary quality of the book is of the same high order as that of the first volume. Although the author is prejudiced in favor of his hero, this does not detract from the quality of the whole.

Introduction to Parasitology with Special Reference to the Parasites of Man. By Asa C. Chandler, M.S., Ph.D., Professor of Biology, Rice Institute, Houston, Texas. Ninth edition. Cloth. $8.50. Pp. 799, with 257 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C.2, England, 1955.

This new edition is an extensive revision of an authoritative and well-known volume first published in 1918. The organization of the text reflects the author's concept that the most desirable approach to the subject of parasitology is a comprehensive integrated account of the entire field. It is not intended to be a definitive textbook for advanced students and highly trained specialists. Following a historical introduction and a chapter dealing with general considerations of parasitism and nomenclature, three major sections deal with the protozoa, worms, and arthropods. The individual species are considered separately and in detail dealing with their structure and physiology and the epidemiology and pathological effects of infestation with them. Recent advances in treatment are well covered. Although the

descriptions of the diseases produced are often insufficient for the purposes of the physician, the information provided is accurate and adequate enough to give a good general picture of the condition. The discussions of epidemiology are particularly good. The many excellent drawings and photographs contribute materially to the value and usefulness of the book, as does the inclusion of a list of basic references at the end of each chapter. The descriptions and discussion of certain parasites of animals add to the general interest of the volume. The style of presentation makes this volume unusually readable for a technical work in this field. One or two typographical errors obscure the meaning of the particular paragraphs they appear in, but such errors are few and far between. A complete index is provided. This book cannot fail to be of interest and use to physicians interested in the fields of medical parasitology and tropical medicine and should be included in all libraries dealing with these subjects.

Faith, Reason and Modern Psychiatry: Sources for a Synthesis. Editor: Francis J. Braceland, M.D., ScD., F.A.C.P. Cloth. $6. Pp. 310. P. J. Kenedy & Son, 12 Barclay St., New York 8, 1955.

Faith, reason, and modern psychiatry seem to be coming closer and closer each year. The newspaper reviews of this subject are increasing in number and depth. Until relatively recently, the viewpoints of religion and psychiatry were contradictory. In the past year, the President of the American Medical Association, Dr. Elmer Hess, was widely quoted in the press as saying that "when the doctor entered the sick room, he did not go in alone." This was a very valuable and important step in the right direction. Much good should come from it. Although until recently, psychiatry was one of the weak links in medicine, it now goes forward rapidly. Some practitioners of medicine have been critical of psychoanalysis, or rather of the interpretation of psychoanalysis. Some believed that it was necessary for psychiatry to begin again with this phase of its work. The present volume is an intelligent approach to the subject by theologians and psychiatrists. The statements of the various writers on both sides are tolerantly and scientifically approached. The reviews by the editor are excellent. No doubt the book will be praised and criticized, but it should act as a much needed bridge between two points of view and should become a useful reference work.

Cough Syncope. By Vincent J. Derbes, M.D., F.A.C.P., Professor of Medicine, Tulane University of Louisiana School of Medicine, New Orleans, and Andrew Kerr, Jr., M.D., Assistant Professor of Medicine, Louisiana State University School of Medicine, New Orleans. Publication number 231, American Lecture Series, monograph in Bannerstone Division of American Lectures in Internal Medicine. Edited by Roscoe L. Pullen, Professor of Medicine and Dean, University of Missouri School of Medicine, Columbia. Cloth. $4.75. Pp. 182, with 7 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1955.

The unusual syndrome cough syncope is well presented. Detailed discussion of the literature, as well as the author's experience is given. Differential diagnosis, related conditions, theories of mechanism, physiological mechanisms, prognosis, medicolegal aspects, and treatment are described, and an extensive bibliography is available. The recognition of cough syncope should be understood by all physicians. The illustrations and tables are clear. This book is highly recommended.

The Science Book of the Human Body. By Edith E. Sproul, M.D. Cloth. $4.95. Pp. 232, with 92 illustrations by Kathleen Elgin. Franklin Watts, Inc., 699 Madison Ave., New York 21, 1955.

Generously illustrated, this volume for nonprofessional readers presents lucid descriptions of the various body systems. Additional special chapters are devoted to the liver, the blood and lymph, metabolism, pregnancy, and the skin. In an introductory chapter, the author describes basic aspects of tissue structure with the varying characteristics, cells and how they function, and the phenomena of growth and repair. The terminology used throughout the volume is appropriate for the indicated reader group. The author has an easygoing, friendly writing style that makes the text run smoothly. An unusual feature is the inclusion, in addition to the many smaller illustrations, of 32 special plates in which relationships of organs are demonstrated for all parts of the body. Among these are illustrations of muscles in action, as well as bones and various types of joints. Other helpful features are an extensive glossary of terms, a bibliography, and a good index. This book can be recommended to patients who want to learn more about the normal functions of their bodies.

Child Behavior. By Frances L. Ilg, M.D., Director, Gesell Institute of Child Development, New Haven, Conn., and Louise Bates Ames, Ph.D., Director of Research, Gesell Institute of Child Development. Cloth. $3.95. Pp. 364. Harper & Brothers, 49 E. 33rd St., New York 16, 1951-1955.

This is a compendium of advice to parents about rearing children in their first 10 years of life. The authors' long training and experience is well reflected in the objectivity of their evaluations and the clarity of their discussions. The principal themes are the processes of human growth and development, considered not in terms of oversimplified Freudian "libidinal phases" but as progressive maturations continuously modifiable by directed experience. Many a harried parent's questions will be answered by the volume without vagueness or dogmatism. The book is enhanced in usefulness by a full index and is recommended as a reliable source of information and guidance in its field.

Introduction to Chemical Pharmacology. By R. B. Barlow, Research Fellow, Yale University School of Medicine, New Haven, Conn. With foreword by H. R. Ing, F.R.S., Reader in Chemical Pharmacology, University of Oxford, Oxford, England. Cloth. $6.25. Pp. 343, with 53 illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Methuen & Co., Ltd., 36 Essex St., Strand, London, W.C.2, England, 1955.

The subject of this book is the relation between chemical constitution and physiological action. As Dr. Ing indicates in the foreword, "It has been a somewhat disappointing subject of study, and some workers have despaired of finding any convincing relationships." That this despair is gradually being dispelled is evidenced by the basic advances in pharmacology in the last 20 years. This timely book considers these advances and their underlying problems after an introductory chapter reviewing basic pharmacological considerations such as the kinetics of pharmacological reactions and mechanism of drug action, the receptor theory, factors influencing drug-receptor complex, sites where drugs act, and other topics related to a full understanding of the subject under discussion. Drugs are classified according to their sites of action, e. g., central nervous system, peripheral nerves, synapses, and certain tissues and organs. Eighteen chapters are devoted to these subjects, followed by a short chapter devoted to the author's conclusions, present knowledge, and predictions for the future. Two appendixes provide brief accounts of anatomy, physiology, and biochemistry to aid those readers without a background in the biological sciences. An index of proprietary drug names and symbols is also appended to aid in identifying agents discussed in the text. The author has provided a concise review of a broad range of pharmacological phenomena. A textbook of this type has been greatly needed. It was primarily written for chemists, but physicians, pharmacologists, and all others interested in the action of changes on biological systems can read it with profit.

Lectures on the Scientific Basis of Medicine. Volume III: 1953-54. British Postgraduate Medical Federation, University of London. Cloth. $6. Pp. 398, with illustrations. John de Graff, Inc., 64 W. 23rd St., New York 10; The Athlone Press, University of London, 2 Gower St., London, W.C.1; distributed by Constable & Co., Ltd., 12 Orange St., London, W.C.2, England, 1955.

The avowed purpose of the annual series of lectures on the scientific basis of medicine is to furnish an integrated survey of current scientific research in relation to clinical medicine and surgery. The lectures published in this volume reflect the growing knowledge of the structure of biological tissues and their reactions to injury, the use of radioisotopes and the method of chromatography, the importance of connective tissues, the actions of enzymes and hormones, infection and immunity, the chemical transmission of nerve impulses, the actions of the anticholinesterases, and experimental dermatology and psychopathology. These authoritative discussions provide a clearer understanding to mature readers of the problems characterizing health and disease.

QUERIES AND MINOR NOTES

SILICOSIS

TO THE EDITOR:—*1. What is the accepted definition of silicosis? 2. How much free silica dust of particles less than 10 μ in diameter can a normal lung handle without deleterious effect? 3. What is the effect on the lung of an individual working in an atmosphere of less than 5 million particles per cubic foot (of harmful size) in which lung there are already signs of silicosis and in which lung there are already signs of tuberculosis? 4. How long does it require for silicosis to develop in a lung under the following general ranges of dust counts of harmful particle size: 10 to 20 million, 50 to 75 million, 100 to 200 million, and 500 million and up? 5. Does the demonstration of a few anisotropic crystals by polarizing microscope in a section of lung tissue make the diagnosis of silicosis? If not, how much silica is required in such sections to make the diagnosis? 6. How much silica by weight in proportion to the weight of the ashed lung is required to make a diagnosis of silicosis? 7. How much silica by weight in proportion to the weight of the ashed lung is required before one can say that it is enough to influence tuberculosis adversely?* *M.D., California.*

ANSWER.—Answers to these concise questions may not be made in equally concise language. Only comment is warranted. 1. Silicosis as a human disease entity may conveniently be defined as one of the pneumonoconioses produced solely by silicon dioxide (silica) in restricted particle size range, in which the characteristic lesion is the silica nodule, which well-established disease in the presence of known exposure usually may be diagnosed by the appearance of the x-ray film and at autopsy by the exhibition of silica nodules; however, at autopsy the majority of adults may reveal a few characteristic nodules with or without industrial exposure. Disability is not determined by the disclosure of characteristic nodule shadows in the x-ray nor by the finding of a few characteristic nodules at autopsy. Well-established and diagnosable silicosis may exist in the absence of disability, and the certainty of disability is provided only through appropriate pulmonary function tests influenced by knowledge of sufficient exposure. In silicosis there are no exact subjective or objective symptoms. 2. Formerly it was believed that all silica particles near to and below 1 μ in size could contribute to the causation of silicosis. Recent work impels the belief that gross exposure to ultramicroscopic-sized particles, that is, particles in size of thousandths of microns, will not induce conventional silicosis but may induce a less severe pulmonary affection with damage chiefly to the surface of pulmonary air passages. Prior to that state of silicosis discernible in the x-ray there must be antecedent pathology, which damage it now is believed may involve the pulmonary capillary bed and with some threat to the total pulmonary circulation. Such and other reservations prevent any exact answer to this question. For practical purposes there is justification to adherence to the concept that long exposures to silica particles in size below 10 μ, in numbers below 5 million particles per cubic foot of air, will not provoke significant or disabling silicosis. 3. Since silicosis once established as here stipulated may progress without any further exposure, it becomes impossible to distinguish between such progression and the effect of continuing minor exposure. On a practical basis obviously at exposure levels well below the 5 million maximum no added threat is expectable. The question as to tuberculosis is only of academic import, since no person with active tuberculosis should be permitted to work. In the instance of healed pulmonary tuberculosis, the previous patient should be permitted to work under the exposure conditions mentioned if accorded judicious medical supervision. 4. Time is a decided variable in silicosis. The majority of workers never will acquire silicosis. With increasing exposures, greater will be the numbers of silicotics and earlier the appearance of the disease. Little exactness is predictable on a time basis. 5. The demonstration of fragments of silica crystals or whole crystals of cryptocrystalline silica only proves exposure, not silicosis. 6. The lung content of silica and other silicon compounds, with and without ashing, has been examined by various methods. The results strikingly are without uniformity. From a series of known silicotics the percentage of free silica in the lung ash runs higher than from a series of lungs from persons without known exposure. In single instances the results may not be conclusive. In one series the percentage of free silica ash ranged from 4.6 to 22.8, while for unimpaired lungs the corresponding range was 1.28 to 4.0%. Lately the matter has become even more complex by disclosure that highly fine particles of silica do not cause silicosis. The determination of silica in lung tissue at autopsy or in life through biopsy may not constitute a valid basis for silicosis diagnosis. 7. It is not known that the incidence of tuberculosis accompanying silicosis is a quantitative affair. Occasionally the belief is encountered that the incidence of tuberculosis along with silicosis is no higher than the general rate of tuberculosis among males of comparable ages in a given community. Certainly it is not established that those ultramicroscopic silica particles causing no silicosis still will not contribute adversely to the frequency of tuberculosis.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

THE WORD "CLINIC"

TO THE EDITOR:—*What is the proper and ethical use of the word "clinic." My own opinion is that its use sprang up in the United States as referring to a group of several doctors each limiting his practice to a specialty; usually there was a close business and professional relationship. In recent years the word is used to apply to the office of one or more doctors, rather loosely associated. In the latter case its use is similar to its use in England. Are both uses proper and ethical?* *M.D., Nebraska.*

ANSWER.—In this country, although the word "clinic" is still applied in some areas to free dispensaries, and is sometimes used to describe a teaching session involving the use of patients, it is most commonly used to connote the pooled efforts and facilities of several physicians practicing together as a group. In the latter sense, so far as can be determined, there are no legal restrictions regarding the number of physicians who must practice together in order to qualify for the use of the word clinic. However, the American Association of Medical Clinics does not admit to full membership any group of fewer than seven full-time physicians nor fewer than five in associate membership. It would appear that there are no specific legal or ethical prohibitions to the use of the word clinic as applied "to the office of one or more doctors, rather loosely associated."

In 1934 the Judicial Council, by resolution, proposed an amendment to the Principles of Medical Ethics. A "whereas" clause of its resolution noted that "groups and clinics were little known, were not serious competition and were not mentioned when the present general revision of the Principles of Medical Ethics were adopted in 1912." The resolution was adopted, and the Principles were revised to include Chapter 1, Section 3, "Groups and Clinics." That section reads in part as follows: "The ethical principles actuating and governing a group or clinic are exactly the same as those applicable to the individual." However, such use of the word clinic for one or two physicians would seem to constitute an attempt to acquire the advantages in public relations that have been given this designation by the reputations of some of the large and well-known groups of physicians.

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TETANUS IMMUNIZATION

To the Editor:—*A 16-year-old boy has been given tetanus antitoxin on two occasions in the past. One week following the first injection he developed generalized urticaria, arthralgia, and mild laryngeal edema. Several hours after the second injection, about one year later, he developed laryngeal edema, urticaria, and a general reaction resembling shock. This was eventually brought under control by means of oxygen, antihistamines, adrenalin, and corticotropin. This boy recently came under my care, and I should like to know if it will be safe to give him tetanus toxoid, to be followed by booster toxoid injections at intervals of several years or as necessitated by injuries.*

M.D., Arizona.

Answer.—Since tetanus toxoid is not a serum product but is the altered toxin product of the tetanus bacillus, it does not give rise to urticaria or serum sickness. In the case under consideration, it would seem advisable to immunize this boy and keep him immunized with booster injections at suitable intervals. There are two methods of accomplishing this. One is the use of the alum-precipitated toxoid given in 0.5 cc. doses. This method requires two injections, one following the other at an interval of four to six weeks. The other method is the use of three doses of 0.5 cc. of fluid toxoid, each given at an interval of three to four weeks. The Navy used the former method; the Army, the latter. Since results were equally good with either method, it would seem to me that one requiring only two injections is to be preferred. Booster injections at the time of injury and at suitable intervals to maintain immunity should be done, and, in the event of injury, no antitoxin should be given.

INDICATIONS FOR HYSTERECTOMY

To the Editor:—*Please send information on the clinical and pathological indications for hysterectomy.*

H. Paul Miller, M.D., Fort Wayne, Ind.

Answer.—The chief indications for hysterectomy are: (1) fibromyomas of the uterus with excessive bleeding; (2) pelvic inflammatory disease necessitating removal of both adnexa (in general, whenever both ovaries must be removed, the uterus should also be extirpated); (3) diseases of the adnexa, such as bilateral dermoid cysts, in cases where normal ovarian tissue cannot be saved and also endometriosis in women past 40 years of age; (4) normal-sized or enlarged uterus due to fibrosis uteri associated with hemorrhage that does not cease after curettage in women past 40 years of age (the ovaries should not be removed); (5) in cases of prolapse of the uterus in elderly women, the uterus is often removed, even though hysterectomy is not essential to the cure of prolapse; (6) carcinoma of the corpus; (7) selected cases of carcinoma of the cervix where a radical operation is to be performed; (8) choriocarcinoma of the uterus; (9) hydatidiform mole in a woman past 45 years of age; (10) sarcoma of the uterus; (11) malignancy of the tubes or ovaries; (12) some cases of severe cervicitis in women past 40 years of age who also have excessive menstruation but not sufficient by itself to justify hysterectomy; (13) dysmenorrhea that does not yield to medication, dilatation of the cervix, and even sympathectomy in women who have had children; (14) stenosis of the cervix from operation or cauterization not curable by dilatation of the cervix and a stem pessary; and (15) as a sterilization procedure rarely at the time of a therapeutic abortion but more often after several cesarean sections.

SELENIUM POISONING

To the Editor:—*Is there any danger to health in the use of selenium rectifiers in electrical instruments in the event of breakage of the rectifier and possible selenium poisoning?*

Michael Bernfeld, M.D., Tucson, Ariz.

Answer.—There is probably little or no health hazard due to the actual breakage of a selenium rectifier as used in electronic apparatus in the home and hospital laboratory. It is possible that when selenium rectifiers are heavily overloaded that fumes containing selenium may be generated. This subject has been considered by Drinker and Nelson (*A. M. A. Arch. Ind. Hyg.* **8**:185-189 [Aug.] 1953). Under conditions of the test reported by these authors, concentrations of hydrogen selenide (H_2Se) of 0.001 ppm developed. The American Conference of Governmental Industrial Hygienists recommends 0.05 ppm as the maximum concentration for eight-hour exposures. It was concluded that in view of many factors that mitigate exposure, such as objectionable odor, ordinary ventilation, brief exposure periods, there is no danger to health of radio and television owners or service men from the occasional accidental burning out of selenium rectifiers.

INDURATION OF CORPORA CAVERNOSA

To the Editor:—*A 40-year-old businessman complained of a posterior curvature of the erect penis of about one month's duration. The onset was gradual and painless. There was no history of trauma. He denies ever having venereal disease. On palpation of the flaccid organ, a definitely calcified mass can be outlined from the base of the penis extending to the glans, on the anterior surface. It corresponds to the location of the corpus cavernosum urethra. There is no tenderness on examination. Blood and urine studies are negative. The prostate is normal to touch, and microscopic examination of the secretion shows only an occasional pus cell. A number 24 French catheter can be passed with ease. A urologist expressed the opinion that this is an unusual form of induration of corpora cavernosa (Peyronie's disease). He felt that neither surgery nor deep x-ray would be of benefit and that the preferred therapy was 40 drops of wheat germ oil daily, given for a year or more. Do you agree, or do you feel that further laboratory study is indicated? This patient is in excellent general health.*

M.D., New York.

Answer.—Judging from the inquiry the penile lesion probably represents a form of induration of corpora cavernosa (Peyronie's disease). The site of the calcified area in the anterior surface of the penis is occasionally observed. Surgical treatment has proved unsatisfactory in most of these cases. Good results have been reported following the application of radium in about 30% of the cases so treated. Favorable results also have been reported following the administration of cortisone. The therapy with wheat germ oil has not gained wide acceptance. The patient can be reassured that this condition is not progressive and that he will gradually accommodate himself to the symptoms present.

FLEETING ERYTHEMATOUS PATCHES AND HIVES

To the Editor:—*A 45-year-old professional man has been under my care for a year. His chief complaint is large patchy erythematous areas often associated with giant hives. At times, these areas look like geometric patterns or like flames from a burner, and they may involve the face. The erythema usually subsides quickly, only to reappear again when the patient is tense, frustrated, or resentful over something in his professional duties. There has never been any involvement of the mucous membrane of the mouth. A short course of hydrocortisone orally last year produced excellent results, but when this medication was discontinued the clinical picture returned. Antihistamine was also tried without effect. Laboratory studies including stool examination, complete blood cell count, sedimentation rate, nonprotein nitrogen studies, and blood sugar level are all within normal ranges; a few visits to an allergist produced no clues. Could you suggest a course of treatment?*

N. W. Nemiroff, M.D., Oradell, N. J.

Answer.—The association of fleeting erythematous patches with giant hives is rather characteristic for the group of toxic or allergic erythematourticarial eruptions. Fleeting erythemas develop where the concentration of liberated histamine is so low that only the first phase of the triple response of Thomas Lewis, the "local vasodilatation," develops. Where higher concentrations of histamine are liberated urticarial wheels or, if the allergic reaction occurs in deeper and larger vessels, giant edema results. This is the explanation for the frequent combination of erythematous patches with urticaria. The geometric configurations of such patterns are due, according to Lewis, to the diffusion of histamine to the periphery and to development of refractoriness in the center. This pattern is most frequently seen in allergic drug eruptions. But there are many cases of "erythema

figuratum" with and without urticaria in which even the most thorough investigation will not unveil the cause. In such cases the condition may last for years. Finally, probably through spontaneous desensitization, the eruption disappears. Emotional impulses often play a provocative role. There is, however, no proof for the rather fashionable assumption that such eruptions are purely psychogenic. If the patient is under psychoanalysis for a year or longer and subsequently gets well, it is impossible to rule out spontaneous termination of the disease. Aggravation under emotional stress is no proof for psychic causation either, only for aggravation by psychogenic vasomotor reaction. Any erythema gets redder if the patient blushes, and histamine has a more intense effect in flushed than in normal skin. The condition can be best controlled by antihistaminics. They are superior to adrenal steroid therapy because in chronic cases, with judicious dosage, they are not so much fraught with the danger of undesirable side-effects. Rarely, true allergy may develop against antihistaminics but in such cases switching to another compound of different chemical composition solves the problem. Periodic general check-ups and white blood cell counts are indicated when antihistaminics are administered over long periods of time.

INVOLVEMENT OF LOWER BRAIN STEM

To the Editor:—*A 65-year-old married woman was in excellent health until 15 months ago when she noted a swelling of her left elbow and forearm that lasted one week and was followed by a weakening of the right wrist, shoulder, elbow, and hand. Three months ago the same sequence followed in the left upper extremity. Two months ago she began to notice a weakening of her legs and in her neck and a dragging type of speech developing. Examination revealed moderate obesity, blood pressure 160/100 mm. Hg, pyorrhea, and slight excoriation of chin suggesting excessive salivation. The neurological examination showed some air conduction deafness of left ear and a lateral nystagmus. Patient's head is carried forward and quickly tires when she tries to hold it up. Shoulder and elbow motions show some weakness. There is complete paralysis of hands. Fasciculations are noted at times in hand muscles, and there is marked atrophy of the thenar muscles. There is some weakness of legs, particularly the left. Reflexes are hyperactive in arms and equivocal in case of abdominals, and Babinski's signs are negative. Blood cell count and urine are normal. Sedimentation rate is 22 mm. per hour (Westergren). The Wassermann has not yet been reported. Is this amyotrophic lateral sclerosis? Please discuss diagnosis and treatment.* *Evarts G. Loomis, M.D., Hemet, Calif.*

Answer.—The patient's symptoms and signs indicate that there is predominantly an involvement of the lower brain stem and cervical spinal cord by a disease process; however, the brief history presented does not warrant a definite diagnosis of amyotrophic lateral sclerosis. Although this illness is a possibility the patient also could have one of the disorders that compress the lower brain stem and upper cervical cord such as platybasia, cervical spondylosis, or a foramen magnum meningioma. The lack of sensory involvement rules out syringomyelia. Further diagnostic studies are indicated, especially lumbar puncture with manometric (Queckenstedt) tests and determination of cerebral spinal fluid protein and serology. The latter also will rule out neurosyphilis. Special x-rays of the skull and cervical vertebra are warranted, especially to check Chamberlain's line (for platybasia) and the foramen magnum for erosion. If there is any suggestion of a cerebrospinal block, a myelogram should be performed. Otherwise a small pneumoencephalogram (using 8 to 12 cc.) might be helpful in ruling out a lesion in or around the fourth ventricle. These procedures are necessary since the disorders considered would be amenable to surgical therapy such as decompression or actual removal of an expanding lesion. If these procedures are all negative, then it is most likely that the patient has an amyotrophic lateral sclerosis with progressive bulbar palsy, and there is no known effective therapy. The prognosis generally is poor with life expectancy varying usually between two and five years after onset. Recently specific treatment has been unsuccessfully tried with vitamin E or alpha tocopherol, vitamin B complex, steroid hormone, and supra vital dyes. Only symptomatic and supportive measures can be given.

SCARLET FEVER

To the Editor:—*My question relates to scarlet fever. The booklet "Control of Communicable Diseases in Man" (an official report of the American Public Health Association), 1955, page 71 B2, states that isolation may be terminated after 24 hour treatment with penicillin, provided therapy is continued for 7 to 10 days. Would a single injection of 600,000 units of benzathine penicillin G (Bicillin) be considered penicillin therapy if continued for 7 to 10 days? In other words, could a case of scarlet fever or family contact be released from isolation 24 hours after a single injection as outlined above?* *Roy G. S. Dougall, M.D., Cobleskill, N. Y.*

Answer.—It does not seem likely that the assertion referred to in the "Control of Communicable Diseases in Man" was intended to imply that a single dose of penicillin, regardless of its magnitude, could be relied upon to free a scarlet fever patient of hemolytic streptococci. The time quoted as a recommended period for penicillin therapy is "7-10 days." In some states the isolation period for uncomplicated scarlet fever is seven days from the onset and there are no restrictions in regard to contacts, nor are there any requirements in respect to medication.

PENICILLIN

To the Editor:—*Are all the Penicillium notatum and its mutations from which penicillin is processed derived from the mold that accidentally contaminated the culture of Dr. Fleming?* *M.D., New York.*

Answer.—The answer to this question is no. The original penicillin that was first prepared for therapeutic use in 1940-1941 was derived from Penicillium notatum. Subsequently strains of P. chrysogenum were used for the production of penicillin because they give a high yield of units of penicillin, and one of these strains, NRRL-1951, was the parent strain from which high-yielding mutants were obtained. In the pharmaceutical industry, experimental work is being carried on continually to isolate and to develop new strains of mutants of Penicillium that will produce higher yields of this antibiotic.

ERYTHROBLASTOSIS

To the Editor.—*A 26-year-old white woman, para 1, grava 2, on Jan. 8, 1955, was about six weeks' pregnant. She and her husband were both Rh negative. She had had no blood transfusions. Her first baby was perfectly normal. On Aug. 18, 1955, she delivered a full-term baby who appeared normal except for a sallow color to its skin. In less than 12 hours this baby was severely jaundiced. A blood cell count revealed 1,400,000 red blood cells per cubic millimeter, and it was Rh positive. The baby's condition appeared critical. A pediatric consultant felt that the baby would not withstand an exchange transfusion but that cortisone and a simple transfusion might help. The baby died while the transfusion was being administered, 13 hours following delivery. How often would you expect Rh difficulty when both parents are Rh negative? What are their chances of trouble with future pregnancies?* *M.D.*

Answer.—When both parents are Rh negative all the children will be Rh negative. In the case cited, therefore, one is dealing either with a child born out of wedlock or with a laboratory error in typing. Usually when both parents are Rh negative one may safely predict that the baby will not be erythroblastotic. In rare cases, however, erythroblastosis can result from A-B-O sensitization or sensitization to some other blood factor such as the Kell factor. The problem in the case described in the query can be resolved only by submitting blood specimens of the father, mother, and their living children to a physician specializing in the field of blood grouping. Since the blood of the erythroblastotic baby who died is no longer available, this may make it more difficult to arrive at an exact diagnosis. At the present stage of knowledge, if a viable erythroblastotic baby is treated promptly and adequately by exchange transfusion, the mortality rate will be less than 5%. For more details see Antenatal Rh Antibody Tests (editorial, *J. A. M. A.* **156:**772 [Oct. 23] 1954).

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RENAL GLYCOSURIA

To the Editor:—*At a conference, renal glycosuria was discussed. In the case presented, all findings were negative, including repeated blood sugar tests. I maintained that this was not a disease entity and that it did not indicate that diabetes mellitus, renal disease, or other organic disease would necessarily result from the renal glycosuria. Exceptions were taken to my viewpoint. What are the current theories on this question?*

M.D., Michigan.

Answer.—Renal glycosuria is defined as the excretion of glucose in the urine at "normal" levels of blood sugar. By "normal" some authorities mean the levels that obtain after an overnight fast, so that in renal glycosuria under these conditions glucose would be present in the urine at all times. Others extend the term renal glycosuria to the condition in which glucose appears in the urine after eating but at blood sugar levels that are appreciably below the average normal renal threshold. In both cases the glycosuria is owing to impairment of the tubular reabsorption of glucose (probably inadequacy of enzymatic phosphorylation), but this may exist and usually does in the absence of any demonstrable renal disease. There is no evidence of which this consultant is aware, despite occasional statements to the contrary, that renal glycosuria leads to renal damage, diabetes mellitus, or any other organic disease. There are cases of true diabetes mellitus with a low renal threshold for glucose. The diagnosis of renal glycosuria should not be made without obtaining simultaneous blood and urine specimens in the course of a standard three-hour glucose tolerance test.

OCCLUSION OF INFERIOR VENA CAVA

To the Editor:—*What are the effects of both sudden and gradual complete occlusions of the inferior vena cava between the renal veins and the hepatic veins? Will ascites result?*

Fred W. Whitehouse, M.D., Boston.

Answer.—There is little knowledge of this particular lesion in the human being. The results from sudden occlusion after ligation in trauma or cancer operations have been, by and large, universally fatal; however, it may be entirely possible that the associated disease may have contributed greatly to these results. The effects of both sudden and complete occlusion of the inferior vena cava between the renal and hepatic veins are well known in the dog, cat, rabbit, and monkey. Death from shock and renal damage occurs after a few hours in almost all animals following complete ligation. Gradual complete occlusions at this level are tolerated very well because of the development of collaterals. Ascites does not develop. Sudden occlusion of the vena cava above the hepatic veins causes death in laboratory animals; however, again gradual occlusion is tolerated well and is associated with ascites. Occlusions of any degree below the renal veins are tolerated in the laboratory animal and in man. Ascites does not occur.

GOUT AND RHEUMATOID ARTHRITIS

To the Editor:—*What are the possibilities of gout and rheumatoid arthritis being present in the same patient at the same time? A 40-year-old male patient continues to be very uncomfortable in spite of the blood uric acid level being reduced to normal with the use of colchicine, Benimid, and Meticorten. The joints most severely involved are the wrists, fingers, ankles, and toes. About the only abnormal finding at present is an elevated blood sedimentation rate.*

Willard W. Van Graafeiland, M.D., Rochester, N. Y.

Answer.—It is possible, but rare, for gout and rheumatoid arthritis to be present in the same patient at the same time. However, it is important to keep in mind that episodic rheumatoid arthritis and polyarticular gout often are confused. The successful reduction of blood uric acid to normal values does not necessarily eliminate the discomfort. The high blood level of uric acid is not the only criterion for discomfort. The routine physical therapeutic procedures for soothing the joints may help in reducing the discomfort of the patient.

REPAIR OF HERNIA DURING PREGNANCY

To the Editor:—*A 27-year-old grava 4, para 3 woman had a repair of an inguinal hernia several years ago, and there has been a recurrence for which a truss was prescribed. The patient is now about 12 to 14 weeks' pregnant, and the hernia is getting larger and causes much discomfort. Is there anything that can be offered this woman in the way of comfort or cure?*

Lester Lando, M.D., Monsey, N. Y.

Answer.—Despite the pregnancy, surgical repair of this hernia should be done. The risk of strangulation, plus the otherwise uncontrollable discomfort, outweigh what little hazard such operation presents to the pregnancy. The further anticipated increase in the abdominal tension should not jeopardize a properly executed repair.

BLOOD DYSCRASIAS IN RADIOLOGISTS

To the Editor:—*What are the dangers to and chances of radiologists developing blood dyscrasias? Can a radiologist doing an average amount of fluoroscopy and wearing apron and gloves be fairly certain of avoiding leukemia in any greater incidence than the average population?*

M.D., Connecticut.

Answer.—There is fairly good evidence that the incidence of leukemia is relatively high in radiologists (March, H. C.: Leukemia in Radiologists, *Radiology* **43**:275-278, 1944), and there is little reason to doubt that excessive exposure to radiation can increase the leukemia rate. Fluoroscopy is one of the most hazardous of the radiologist's occupations, and there is no practical means of making it absolutely safe. With imperfect apparatus and an inexperienced operator, the body dose is apt to be high, even if gloves and an apron are worn. To assure a reasonable degree of safety, it is necessary to check the fluoroscope carefully for stray radiation, work with a small shutter opening, a low milliamperage, and a minimum observation time. In addition to technical precautions, it is important that the radiologist be experienced and that his eyes be well accommodated to the dark.

PARASYMPATHETIC ATONY OF BLADDER

To the Editor:—*Is there another drug that may be used orally in place of furmethide tablets for a parasympathetic stimulant for urinary bladder weakness as in poliomyelitis? If so, who is the manufacturer?*

E. S. King, M.D., Shelby, N. C.

Answer.—Of the several parasympathetic stimulants used with atony of the urinary bladder, Urecholine chloride is most frequently employed. This drug was introduced by Merck & Company, Inc., Rahway, N. J., and is distributed by Sharp and Dohme, Division of Merck & Co., Inc., Philadelphia. Although such stimulants are sometimes accompanied by disagreeable sensations, such as flushing of the face, headache, and dizziness, no serious complications have been reported from their use. In cases of this kind, it would be well to exclude the possibility of any tissue obstruction at the bladder neck, which sometimes develops following parasympathetic atony.

CORTISONE AND SPONDYLITIS

To the Editor:—*Is cortisone of value in the treatment of hypertrophic spondylitis in a 47-year-old male?*

M.D., New York.

Answer.—The majority of patients who have hypertrophic spondylitis (osteoarthritis of the spine) do not derive sufficient benefit from the use of cortisone to justify the risk and expense of its prolonged systemic administration. Occasionally the brief use of cortisone has served to afford some relief for acute exacerbations of this condition; nevertheless, such exacerbations as well as the more chronic symptoms generally are best treated by other measures, such as physical therapy, salicylates, increased rest, limited use of the back, the use of a firm bed, and sometimes a suitable brace for the spine.

SECTION ON GASTROENTEROLOGY AND PROCTOLOGY

BILLINGS GOLD MEDAL

Esophagitis

A Common Condition Frequently Overlooked

Herbert W. Schmidt, M.D.
Section of Medicine

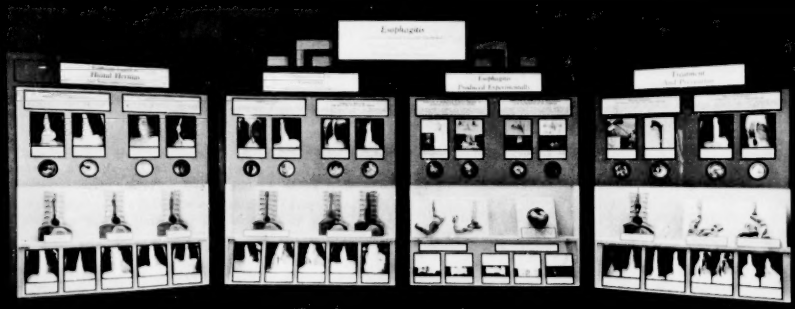
Arthur M. Olsen, M.D.
Section of Medicine

F. H. Ellis, Jr. M.D.
Section of General Surgery

John H. Grindlay, M.D.
Section of Surgical Research

Arthur H. Bulbulian, M.S.
Museum of Hygiene and Medicine

Mayo Clinic and Mayo Foundation



Esophagitis is a relatively common disorder that is frequently overlooked. It usually occurs in association with conditions that produce or permit regurgitation of gastric contents. Thus, the causes of vomiting may be etiologic factors in the production of esophagitis.

Incompetence of the sphincteric mechanism at the cardia is also a very important factor. Such cardial incompetence occurs frequently with esophageal hiatal hernia and as a complication of surgical procedures that destroy the cardial mechanism.

This exhibit presents (1) typical case reports illustrating various conditions producing esophagitis, (2) pathologic specimens, photomicrographs and esophagoscopic photographs of esophagitis in man, (3) methods for the experimental production of esophagitis and surgical technics designed to prevent esophagitis and (4) various methods of treating esophagitis and its complications.

This is one of the many exhibits shown at the June, 1955, meeting of the American Medical Association and which have been collected for pictorial presentation in the "A.M.A. Scientific Exhibits 1955." This book is published by Grune & Stratton, Inc., N. Y. These exhibits are published in their entirety and are not abstracts.

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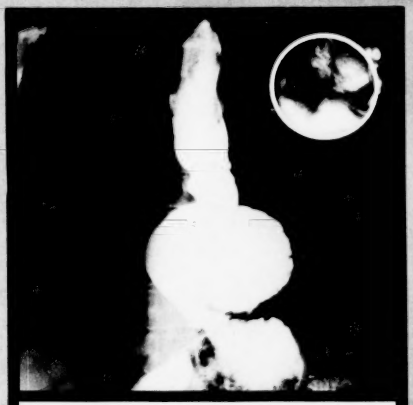
Esophagitis Caused by **Hiatal Hernias** *and Some Other Conditions*

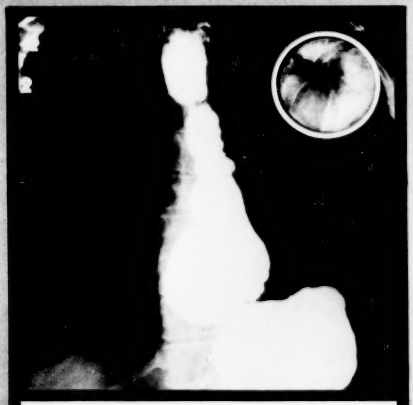
Esophagitis Caused by Esophageal Hiatal Hernia in Adults

Displacement of the esophagogastric junction into the thorax, causes incompetent cardia allowing regurgitation of gastric secretions. Hydrochloric acid and digestive enzymes are responsible for peptic esophagitis. Ulcerations of the esophageal mucosa will develop and heal and eventually cicatricial changes will occur. The esophagus may shorten and in many cases stricture may be the end result.



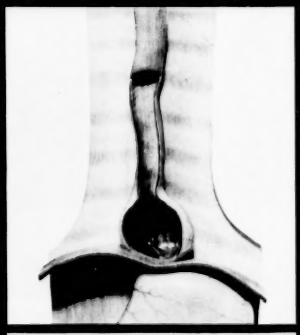
Hiatal Hernia With Ulcerative Esophagitis

A 60-year-old woman with hiatal hernia, duodenal ulcer, gallstones and long-standing dyspepsia. Esophagoscopy disclosed severe ulcerative esophagitis. Hiatal hernia repaired and stomach brought below diaphragm.

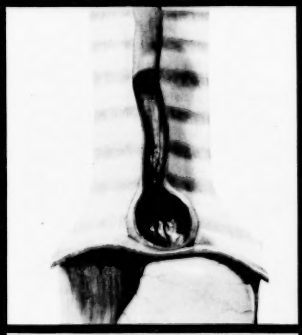


Healed Esophagitis With Cicatrization 3 Years Later

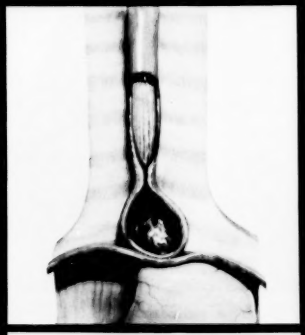
Same patient returned nearly 3 years later with complaint of dysphagia of 1 year's duration. Esophagitis had healed with marked shortening of the esophagus, stricture formation and resultant intrathoracic stomach.



Sliding Type of Hiatal Hernia



Incompetence of Cardia Leads to Esophagitis



Healing of Esophagitis Produces Stricture

Esophagitis Caused by Incompetent Cardia in Children

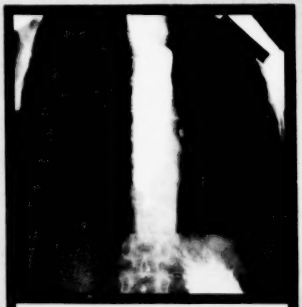
Regurgitant esophagitis may occur in newborn infants. Incompetence of the cardia seems to be responsible. Some children are born with congenital hiatal hernia; others are born with congenital short esophagus. In either case, cicatricial changes are common and serious dysphagia is present. Early recognition and proper treatment of incompetence of the cardia in children are most important.

Congenital Short Esophagus

A congenital short esophagus with stricture at the esophagogastric junction in a child 1 year of age who had had difficulty in swallowing since birth.

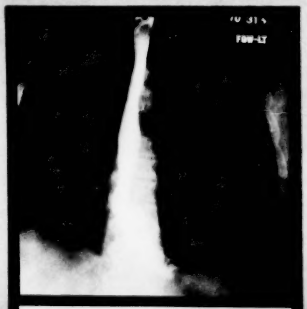
Esophagitis and Stricture

A 5-year-old girl was found to have a short esophagus, esophagitis and stricture. History of regurgitation when lying down since early infancy. Patient was observed for 5 years and the esophagus was dilated 30 times.



Esophageal Ulcer and Stricture Secondary to Cardiospasm

A 59-year-old man had cardiospasm and esophagitis which progressed to a short esophagus with ulceration and stricture at the esophagogastric junction.



Esophageal Ulcer Secondary to Diaphragmatic Hernia

Esophageal hiatal hernia with associated incompetency at the cardia allowed gastric regurgitation into the distal esophagus and produced a deep ulcer. The ulcer eroded into an artery and produced fatal hemorrhage.

Esophagitis and Carcinoma

This 63-year-old woman had symptoms of regurgitation for 6 years and dysphagia for 4 years. Carcinoma developed in a hiatal hernia and the lesion proved to be inoperable at exploration.

Esophagitis Caused by **Vomiting** *and Surgical Procedures*

Esophagitis Caused by Vomiting

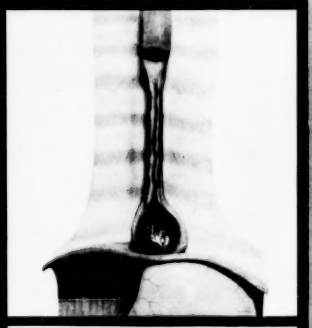
Prolonged vomiting may produce peptic esophagitis with ulceration. Inflammation is diffuse throughout the esophagus. Resulting strictures are frequently very long and the cicatricial changes often produce a short-esophagus type of hiatal hernia. Vomiting of pregnancy, vomiting from pyloric or intestinal obstruction and post-operative regurgitation are frequent causes of ulcerative esophagitis.

Esophagitis Caused by Vomiting of Pregnancy

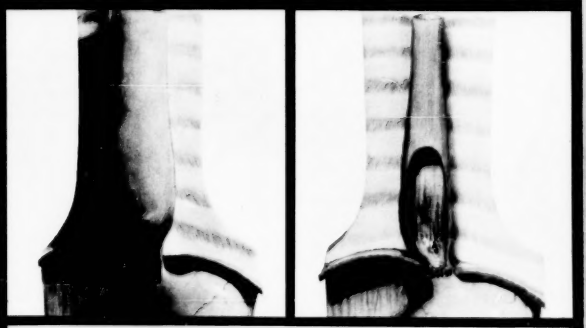
A 29-year-old woman experienced severe prolonged vomiting associated with toxemia of pregnancy and jaundice. Severe esophagitis and an elongated esophageal stricture with intrathoracic stomach developed.

Esophagitis Caused by Postoperative Vomiting

A 73-year-old man had obstructing carcinoma of the colon. Much vomiting and prolonged nasal tube drainage before operation. Severe ulcerative esophagitis and an elongated stricture with intrathoracic stomach developed.



Vomiting Produces Diffuse Esophagitis and a Long Stricture



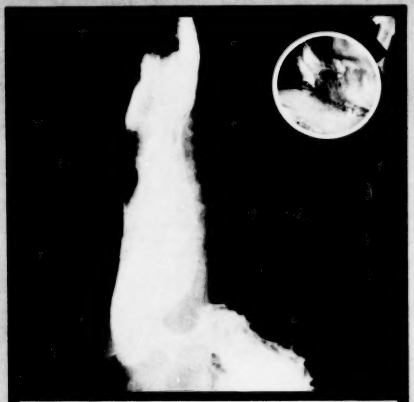
Cardioplasty for Cardiospasm (Wendel technic) Relieves Obstruction but Renders the Cardia Incompetent: Regurgitation Causes Esophagitis and Ulceration

Esophagitis Resulting From Operations Involving the Cardia

Operative procedures which destroy or bypass the cardiac mechanism result in regurgitation of gastric secretion. Esophagitis is a frequent sequela of procedures such as esophagogastrectomy and cardioplasty. Alkaline esophagitis may develop after total gastrectomy with either esophagoduodenostomy or esophagojejunostomy.

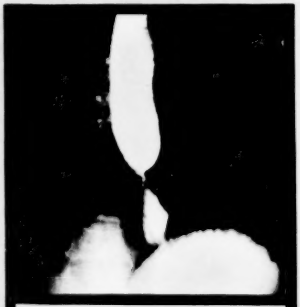
Esophagitis Following Esophagogastrectomy for Carcinoma

A 34-year-old man. Dysphagia, epigastric burning and regurgitation developed 4 months after esophagogastrectomy for carcinoma of the esophagus. Severe esophagitis and stricture resulted 1 year later.



Esophagitis Following Cardioplasty for Cardiospasm

A 34-year-old man. Massive hemorrhage and anemia following cardioplasty (Wendel) performed elsewhere 10 months previously. Esophagoscopy revealed ulcerative esophagitis.



Esophagitis Secondary to Duodenal Ulcer

A 58-year-old man with hiatal hernia, obstructing duodenal ulcer and ulcerative esophagitis. Stricture of esophagus over period of 3 years.

Esophagitis Following Esophagogastrostomy

Hemorrhagic esophagitis with stricture in a 46-year-old man 3½ years following esophagogastrostomy (Grondahl) for cardiospasm.

Esophagitis Following Cardioplasty

A 44-year-old woman with esophagitis following cardioplasty (Wendel) for cardiospasm. Esophagogastrectomy subsequently elsewhere, with fatal esophageal hemorrhage.

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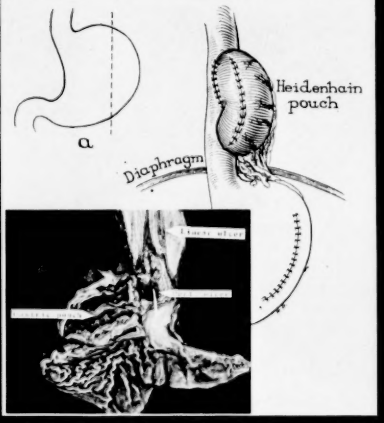
Esophagitis Produced Experimentally

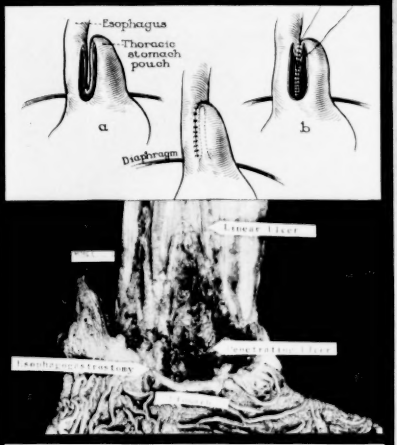
Production of Esophagitis by Direct Exposure of Esophagus to Acid Gastric Secretions

Work done in collaboration with H. R. Ripley, Fellow, Mayo Foundation

Experimental esophagitis was produced in dogs by exposing the esophagus to the acid gastric secretions. In one method, a portion of the stomach was transferred to the esophagus and its secretions made to drain into the esophagus (Heidenhain pouch). In another method, the cardial mechanism was made inactive by esophagogastrostomy, which permitted regurgitation of gastric contents.



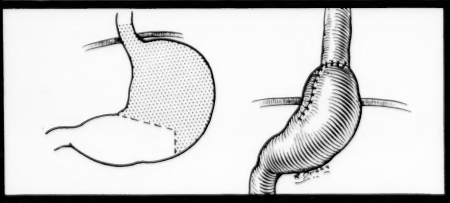
Experimental implantation of a Heidenhain pouch into the esophagus of dogs caused severe ulcerative esophagitis.



Severe esophagitis was also produced following experimental esophagogastrostomy of the Grondahl type.

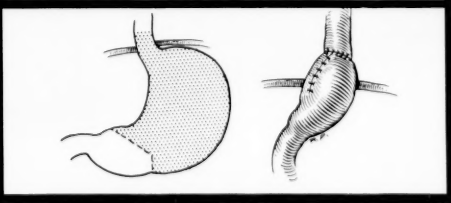
Experimental Esophagogastrectomy

Work done in collaboration with R. T. Hood, Jr., Fellow, Mayo Foundation



Esophagitis Develops

Esophagitis develops in experimental esophagogastrectomy in dogs if some acid-secreting portion of the stomach is allowed to remain.



Esophagitis Rarely Develops

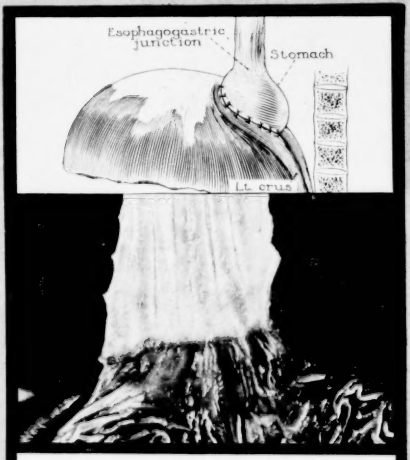
Esophagitis rarely develops if all the acid-secreting portion of the stomach is resected and the esophagus is anastomosed to the antrum.

Esophagitis Produced Experimentally (Cont.)

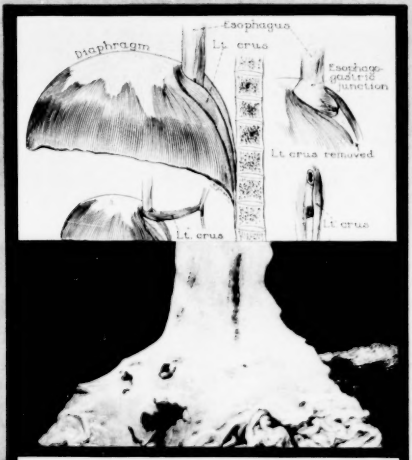
Production of Esophagitis by Interference With the Mechanism of the Diaphragm

Work done in collaboration with V. J. Giuseffi, Jr., Fellow, Mayo Foundation

Intact diaphragm helps maintain competence of the cardia. Incompetence of cardia was produced by two methods. In one set of experiments, competence of cardia was destroyed by production of esophageal hiatal hernia and in another set of experiments by removal of the left crus of the diaphragm. In both experiments, esophagitis developed in a large number of dogs due to regurgitation of acid gastric contents.



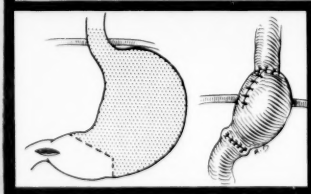
Canine esophagitis resulting from experimentally produced esophageal hiatal hernia showing the inflammatory reaction along the esophagogastric junction and ascending the esophagus in a typical linear pattern.



Canine esophagitis resulting from interference with the diaphragmatic pinchcock mechanism by surgical excision of the left crus of the diaphragm.

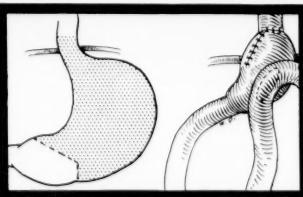
Types of Drainage Procedures in Conjunction With Esophagogastrectomy and Esophagoantrostomy

Work done in collaboration with H. W. Neuman, Fellow, Mayo Foundation



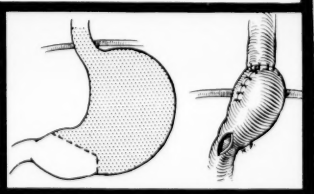
Heineke-Mikulicz Pyloroplasty

When a Heineke-Mikulicz pyloroplasty is used for drainage, alkaline regurgitation leads to ulcerative esophagitis.



Gastroenterostomy

When gastroenterostomy is used for drainage, alkaline regurgitation leads to ulcerative esophagitis.



Extramucosal Pyloromyotomy

When extramucosal pyloromyotomy is used for drainage, ulcerative esophagitis due to alkaline regurgitation is minimized.

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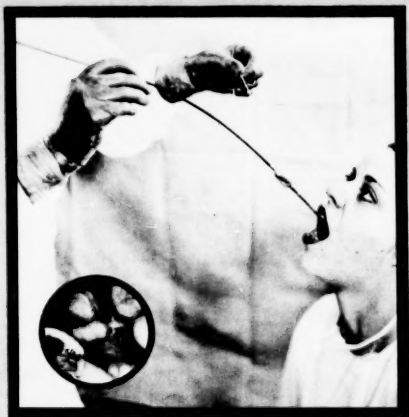
Treatment and Prevention

Medical Treatment of Esophagitis and Its Complications

Medical treatment of esophagitis and its complications should include: (1) ulcer diet, (2) prevention of regurgitation by (a) elevation of head of bed and (b) reduction of pressure within the abdomen by weight reduction and avoidance of tight garments, (3) neutralization of gastric acids by regular use of antacids and (4) dilation of esophageal strictures by mechanical means.

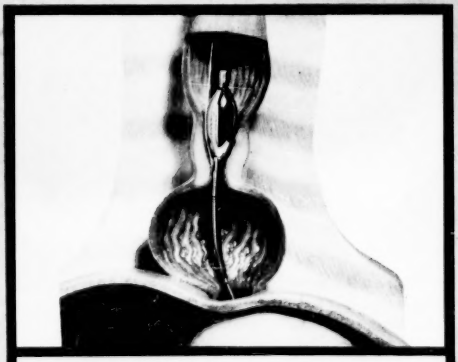


Thread Serves as a Guide

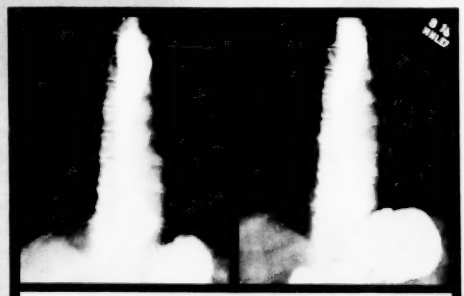
This method of dilation utilizes a previously swallowed thread. Fifteen feet of thread is swallowed at the rate of 12 inches per hour and is engaged in the small bowel.

Dilating the Stricture

Passage of the wire spiral and sounds over the thread is accomplished with the aid of a flexible whalebone staff. Graduated sounds up to 45 French are passed through the stricture.



Esophageal Stricture Being Dilated
(See photographs above)



Esophageal Stricture Successfully Treated by Dilation

A 60-year-old man. Stricture of esophagus caused by regurgitation following operation for carcinoma of the colon (left). The stricture was treated successfully by means of a series of dilations (right).

Treatment and Prevention (Cont.)

Surgical Treatment of Esophagitis and Its Complications

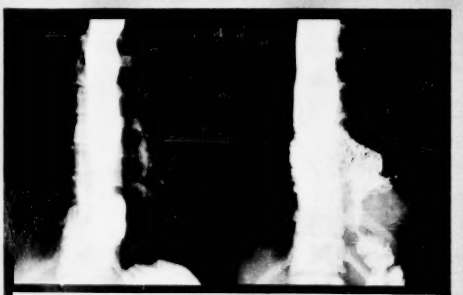
Esophagitis caused by hiatal hernia is best treated by reduction of the hernia. Complications of esophagitis may be successfully treated by (1) extensive esophagogastrectomy and pyloromyotomy, (2) Roux-Y esophagojejunostomy. Subtotal gastrectomy, transplantation of esophagogastric junction to dome of diaphragm and interposition of a limb of jejunum between stomach and esophagus have also been used.

Esophageal Stricture Following Esophagogastrectomy

Patient treated elsewhere 12 months previously by resection of the cardia and esophagogastrostomy for cardiospasm. Severe ulcerative esophagitis with stricture developed 8 months later.

Condition Relieved Surgically

Extensive esophagogastrectomy with removal of all the stomach down to the antrum and an extramucosal pyloromyotomy. One year later, patient had gained 40 pounds and was asymptomatic.



Esophageal Stricture Treated by Esophagojejunostomy

A 47-year-old woman. Short-esophagus diaphragmatic hernia with ulceration and stricture (left). Treated by limited esophagogastric resection and esophagojejunostomy (Roux-Y). Pain and dysphagia relieved 6 months later (right).

Transplantation of Esophagogastric Junction to the Dome of the Diaphragm

A 60-year-old woman. Diaphragmatic hernia of 11 years' duration. Despite medical treatment, short esophagus developed with bleeding (left). Treated by paralysis of the left diaphragm and transplantation of esophagogastric junction to dome of diaphragm. No further bleeding 2 years later (right).

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